BEST AVAILABLE IMAGES

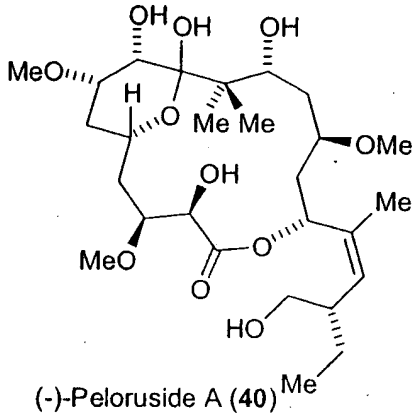
Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

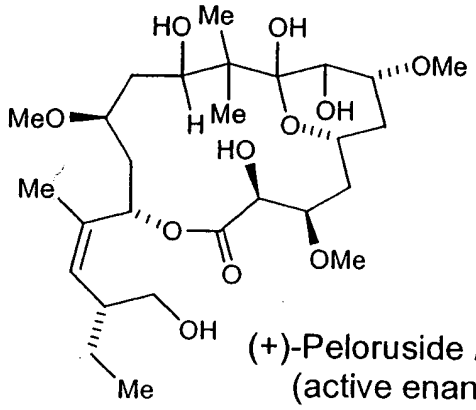
IMAGES ARE BEST AVAILABLE COPY.

As rescanning documents *will not* correct images, please do not report the images to the Image Problem Mailbox.



(-)-Peloruside A (**40**)

FIG. 1



(+)-Peloruside A (**ent-40**)
(active enantiomer)

FIG. 2

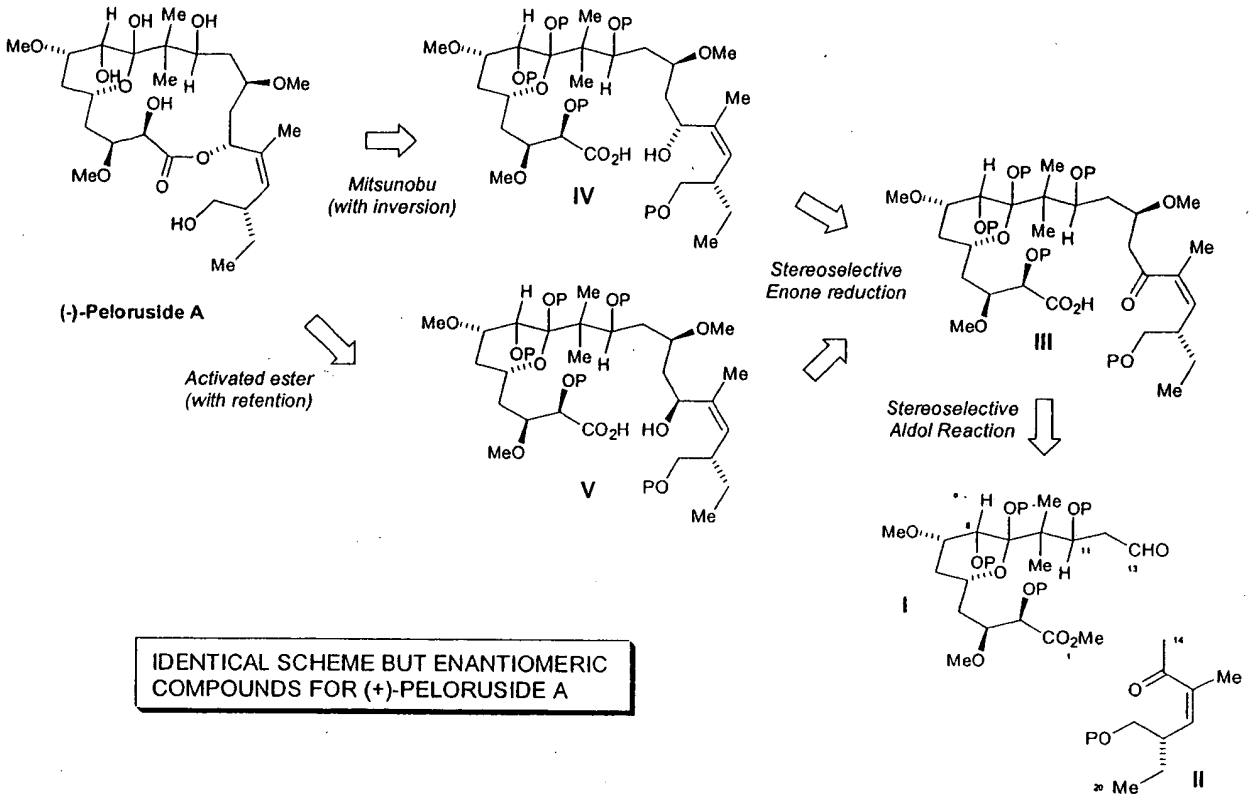

(-)-Peloruside A
Mitsunobu
(with inversion)
IV
Activated ester
(with retention)
V
Stereoselective
Enone reduction
III
Stereoselective
Aldol Reaction
I
II
IDENTICAL SCHEME BUT ENANTIOMERIC
COMPOUNDS FOR (+)-PELORUSIDE A

FIG. 3

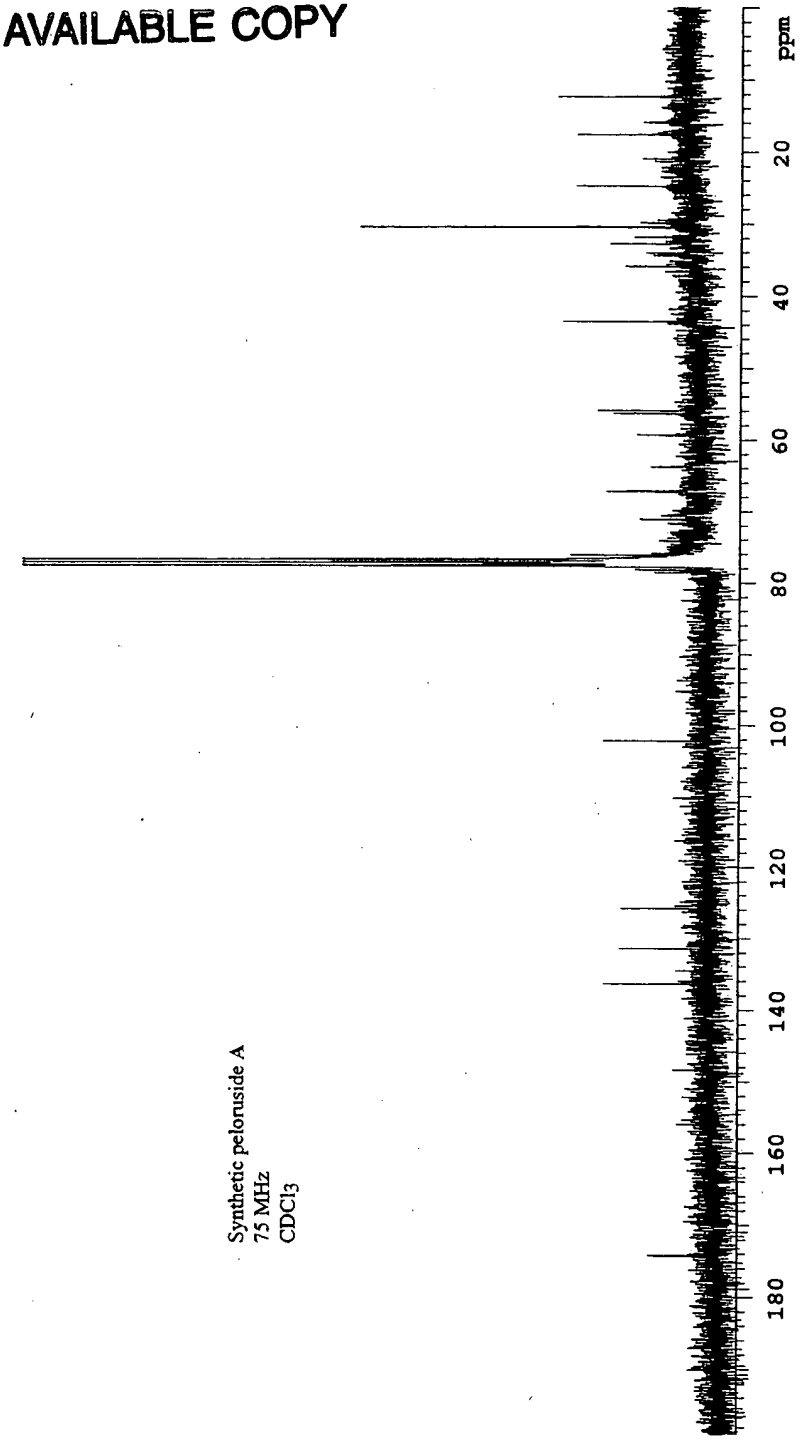


FIG. 4

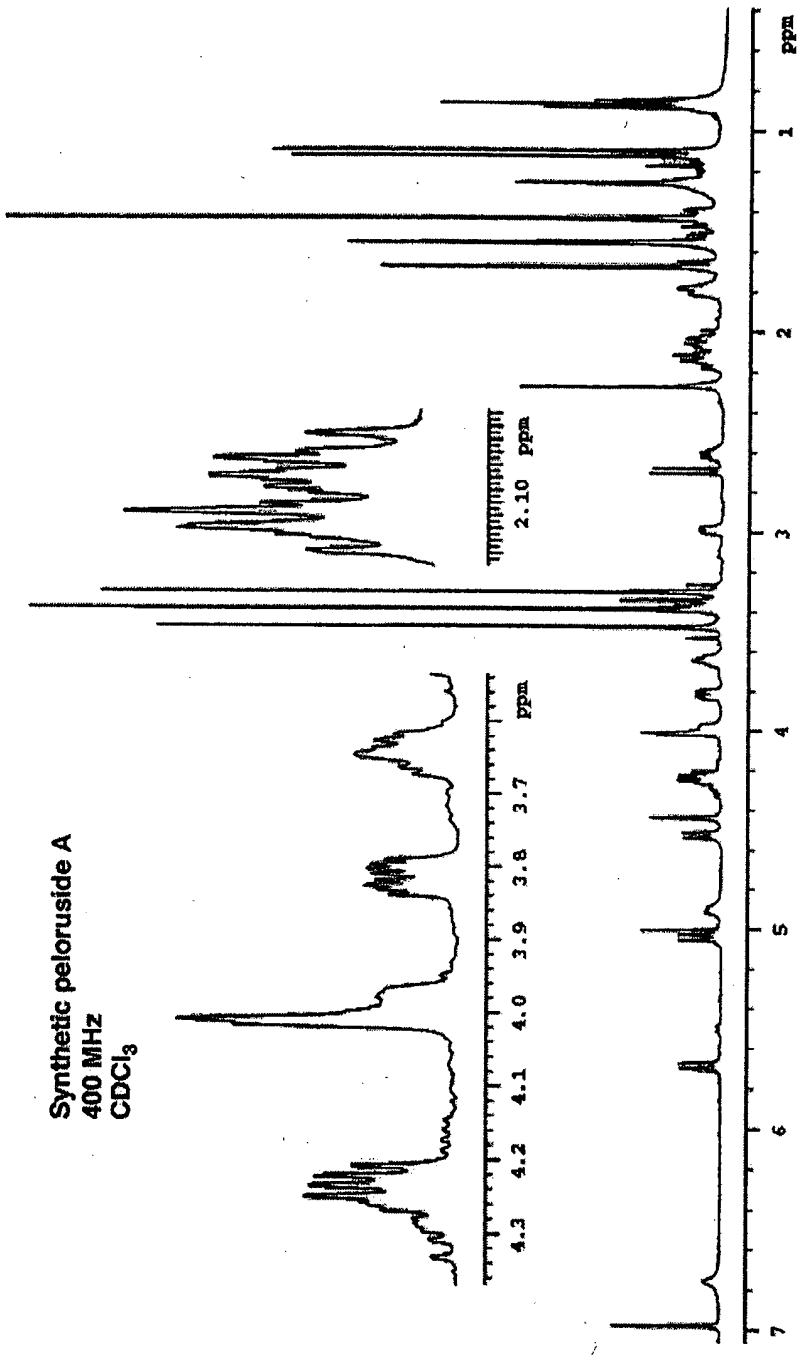

Synthetic peloruside A
400 MHz
$CDCl_3$
4.3
4.2
4.1
4.0
3.9
3.8
3.7
ppm
2.10 ppm
7
6
5
4
3
2
1
ppm

FIG. 5

C1-C13 Fragment:

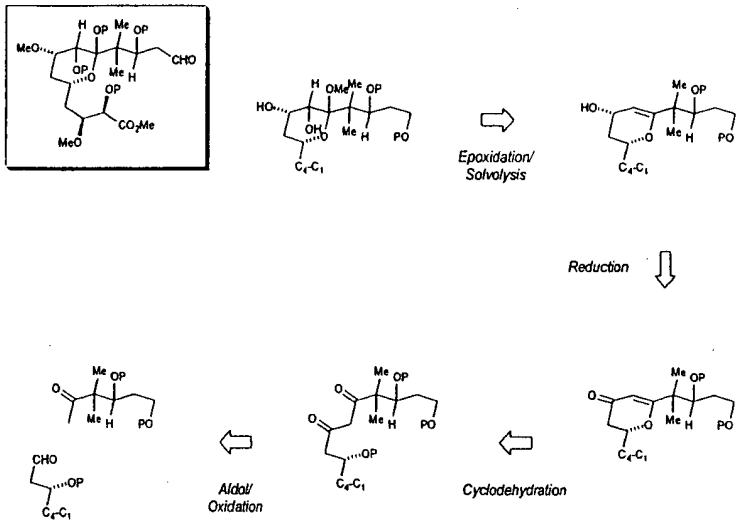


FIG. 6

C1-C13 Fragment: Problematic Glycal-Epoxide Solvolysis

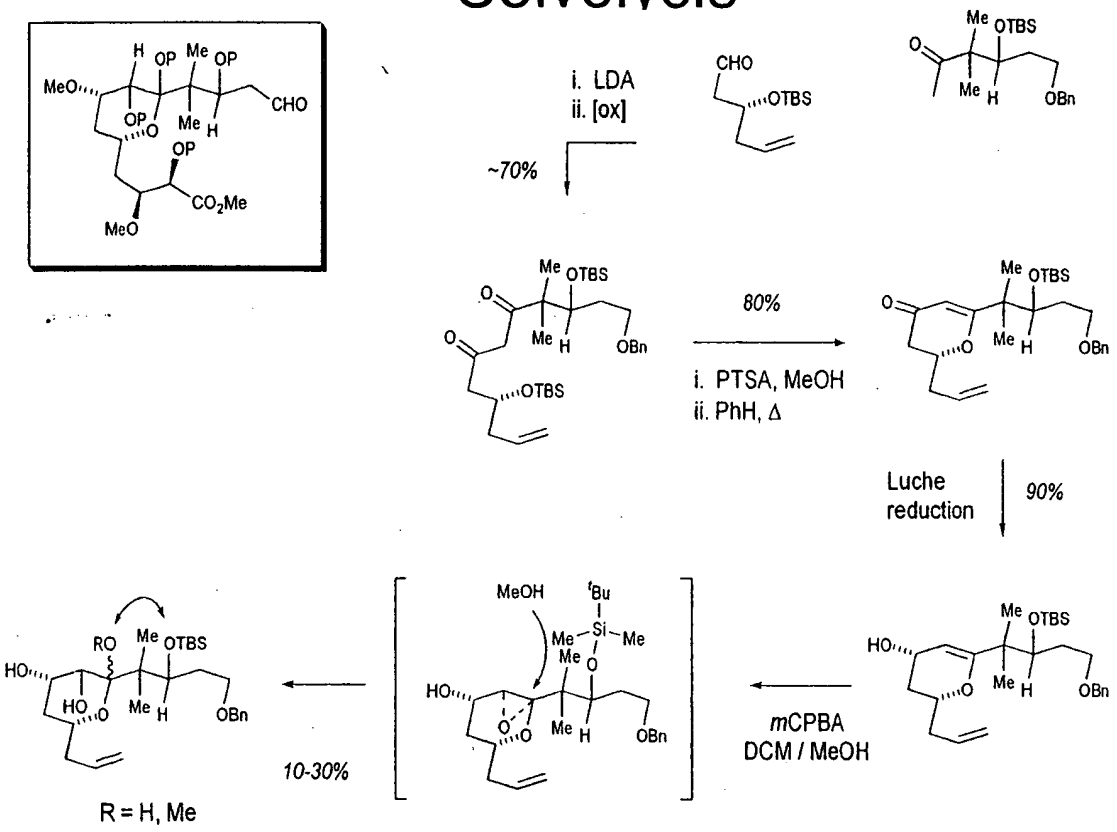


FIG. 7

Solution: Eliminate C11 Stereogenic Centrum

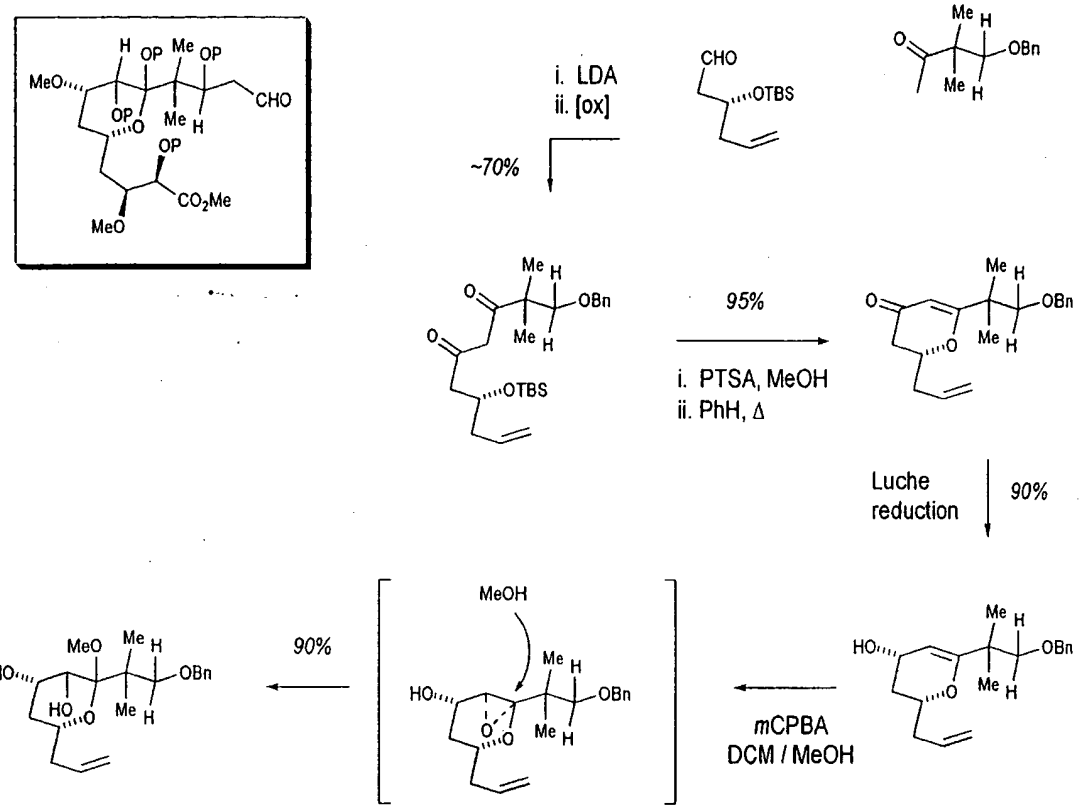


FIG. 8

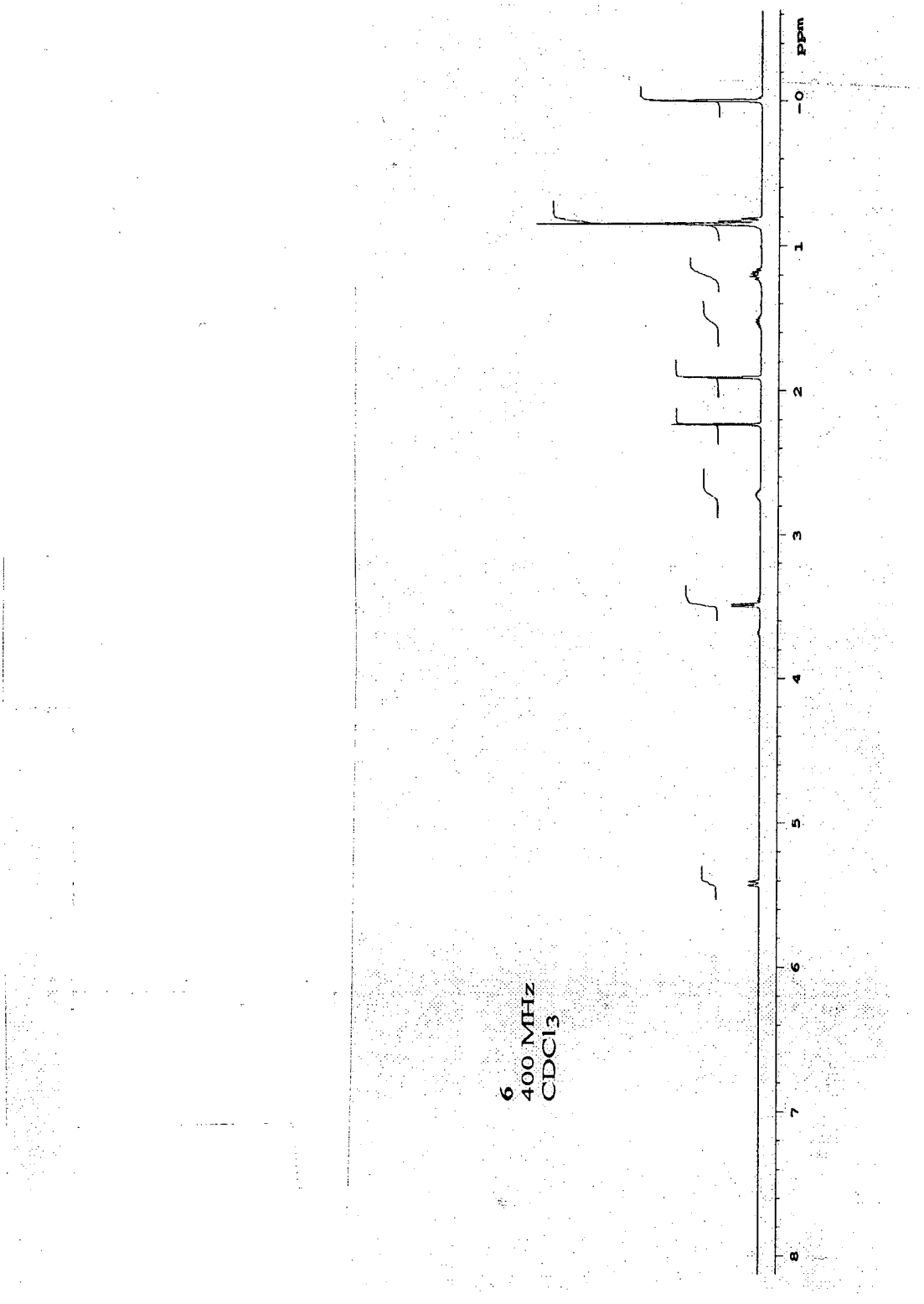


FIG. 9

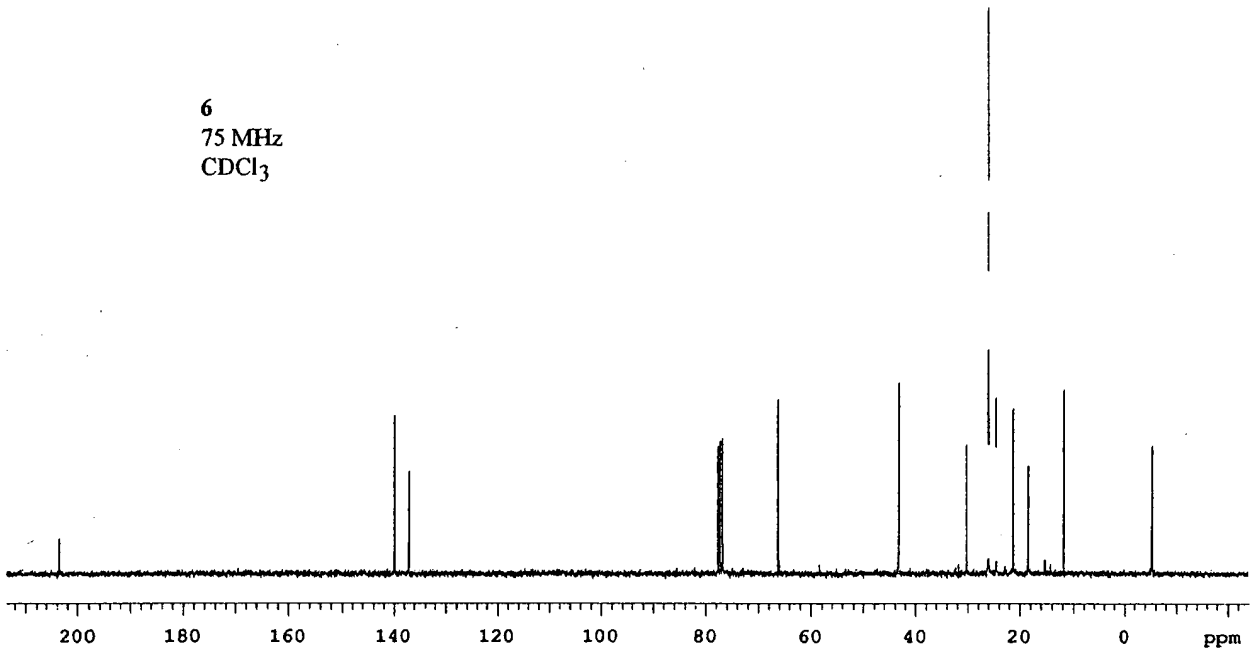


FIG. 10

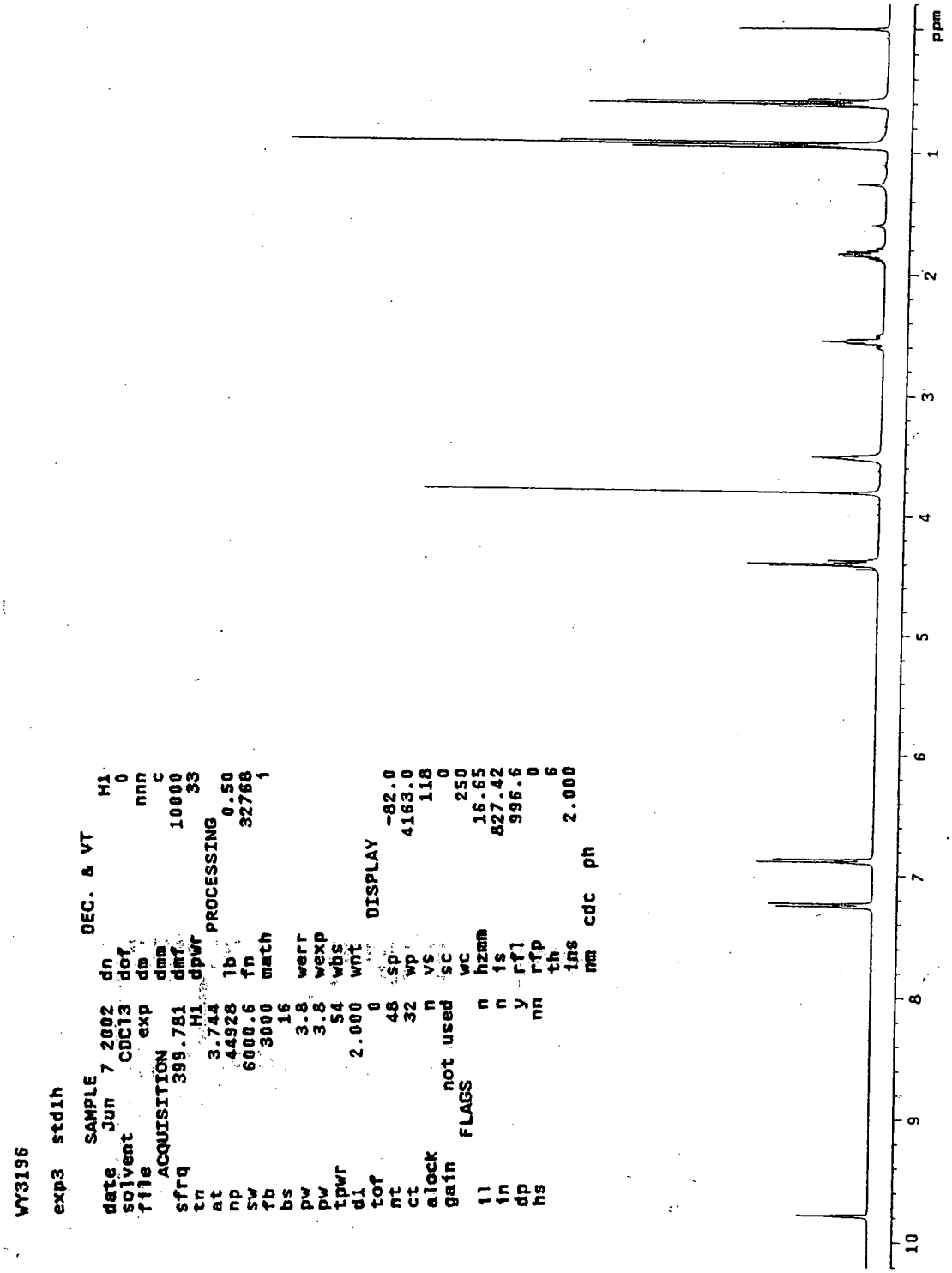

WY3196
exp3 stdih
SAMPLE
date Jun 7 2002
solvent CDCl3
file exp
ACQUISITION
sfrq 399.781
tn H1
at 3.744
np 44928
sw 6000.6
fb 3000
bs 16
pw 3.8
pw 3.8
tpwr 54
d1 2.000
tof 0
nt 48
ct 32
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DEC. & VT
dn H1
dof 0
dm nnn
dmm c
dmf 10000
dpwr 33
PROCESSING
lb 0.50
fn 32768
math 1
werr
wexp
wbs
wnt
DISPLAY
sp -82.0
wp 4163.0
vs 118
sc 0
wc 250
hzmm
is 16.65
rfl 827.42
rfp 996.6
th 0
ins 6
2.000
nm cdc ph
ppm
1
2
3
4
5
6
7
8
9
10

FIG. 11

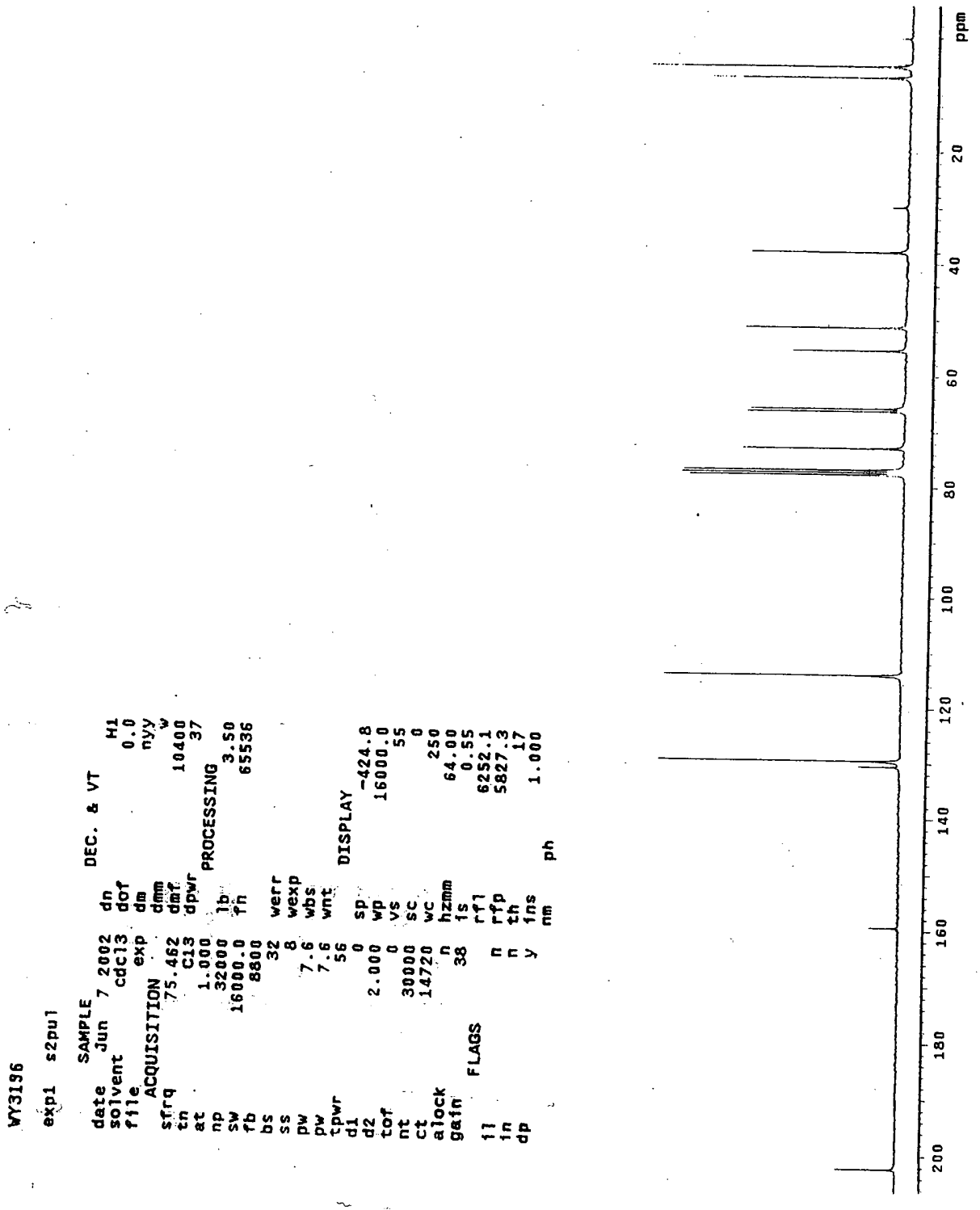

WY3196
exp1 s2pul
SAMPLE
date Jun 7 2002
solvent cdcl3
file
ACQUISITION
sfrq 75.462
tn C13
at 1.000
np 32000
sw 16000.0
fb 8800
bs 32
ss 8
pw 7.6
pw 7.6
tpwr 56
d1 0
d2 2.000
tof 0
nt 30000
ct 14720
alock n
gain 38
FLAGS
11 n
in n
dp y
DEC. & VT
dn H1
dof 0.0
dm nyy
dmm w
dmf 10400
dpwr 37
PROCESSING
lb 3.50
fn 65536
werr
wexp
wbs
wnt
DISPLAY
sp -424.8
wp 16000.0
vs 55
sc 0
wc 250
hzmm
fs 64.00
rfl 0.55
rfp 6252.1
th 5827.3
ins 17
nm 1.000
ph
200
180
160
140
120
100
80
60
40
20
ppm

FIG. 12

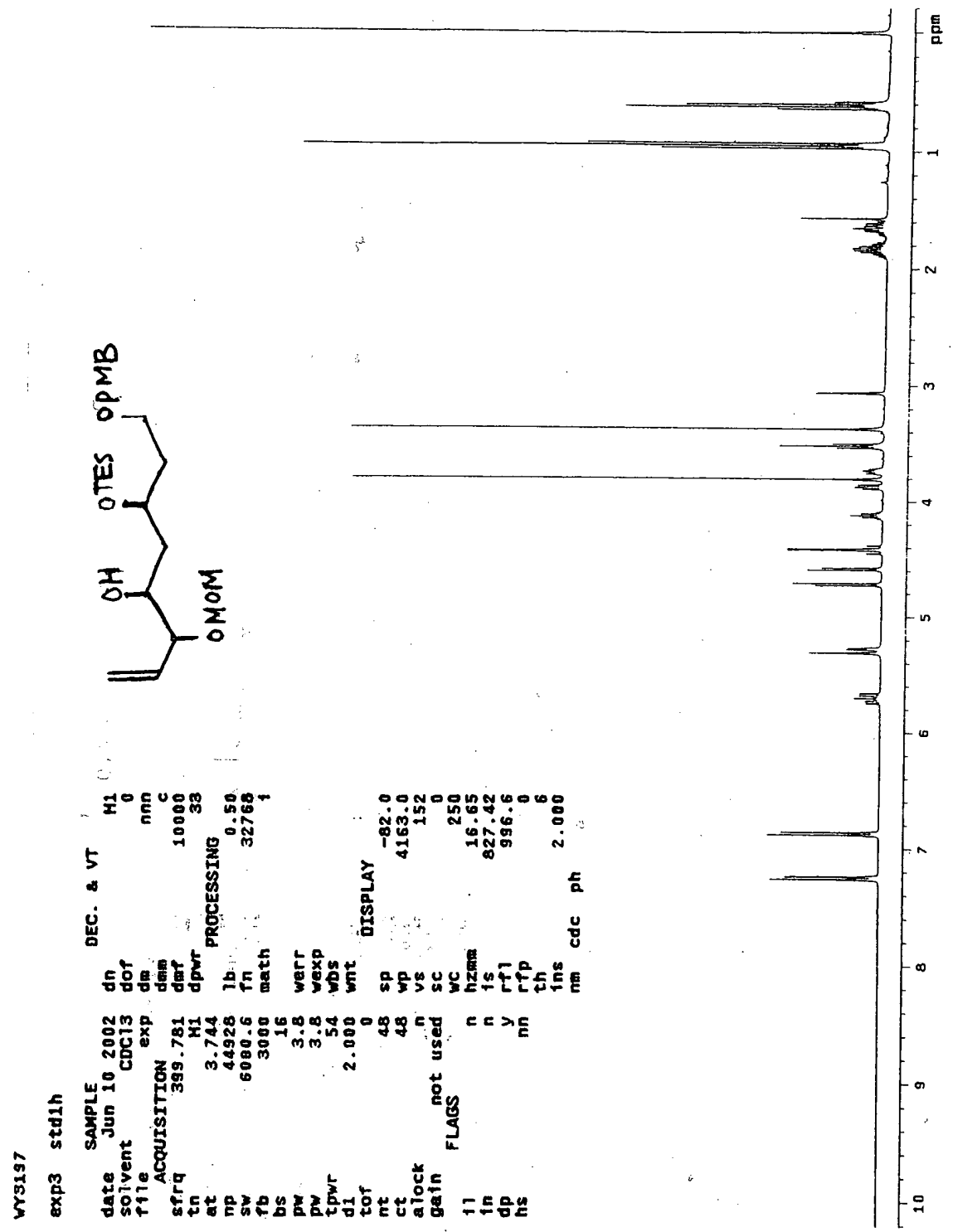

OPMB
OTES
OH
OMOM
VY3197
exp3 std1h
SAMPLE
date Jun 10 2002
solvent CDCl3
file exp
ACQUISITION
sfrq 399.781
tn H1
at 3.744
np 44928
sw 6000.6
fb 3000
bs 16
pw 3.8
pw 3.8
tpwr 54
d1 2.000
tof 0
nt 48
ct 48
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DEC. & VT
dn H1
dof 0
dm nnn
dmm c
dmf 10000
dpwr 33
PROCESSING
lb 0.50
fn 32768
math 1
werr
wexp
wbs
wnt
DISPLAY
sp -82.0
wp 4163.0
vs 152
sc 0
wc 250
hzmm 16.65
is 827.42
rfl 996.6
rfp 0
th 6
ins 2.000
nm cdc ph
ppm
1
2
3
4
5
6
7
8
9
10

FIG. 13

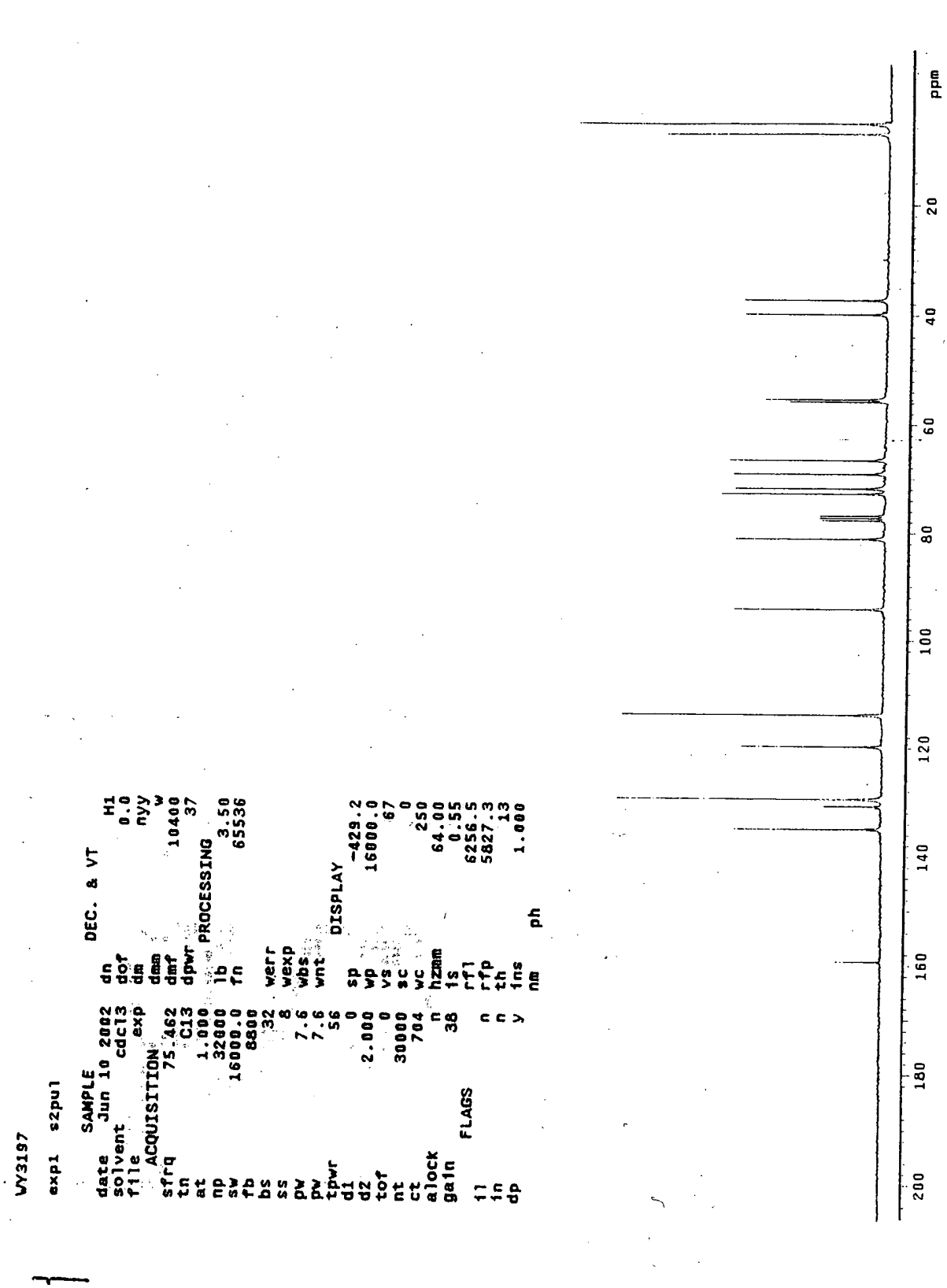

WY3197
exp1 s2pul
SAMPLE
date Jun 10 2002
solvent cdcl3
file exp
ACQUISITION
sfrq 75.462
tn C13
at 1.000
np 32000
sw 16000.0
fb 8800
bs 32
ss 8
pw 7.6
pw 7.6
tpwr 56
d1 0
d2 2.000
tof 0
nt 30000
ct 704
alock n
gain 38
FLAGS
il n
in n
dp y
DEC. & VT
dn H1
dof 0.0
dm nyy
dmm w
dmf 10400
dpwr 37
PROCESSING
lb 3.50
fn 65536
werr
wexp
wbs
wnt
DISPLAY
sp -429.2
wp 16000.0
vs 67
sc 0
wc 250
hzmm 64.00
is 0.55
rfl 6256.5
rfp 5827.3
th 13
ins 1.000
nm ph
ppm
200
180
160
140
120
100
80
60
40
20

FIG. 14

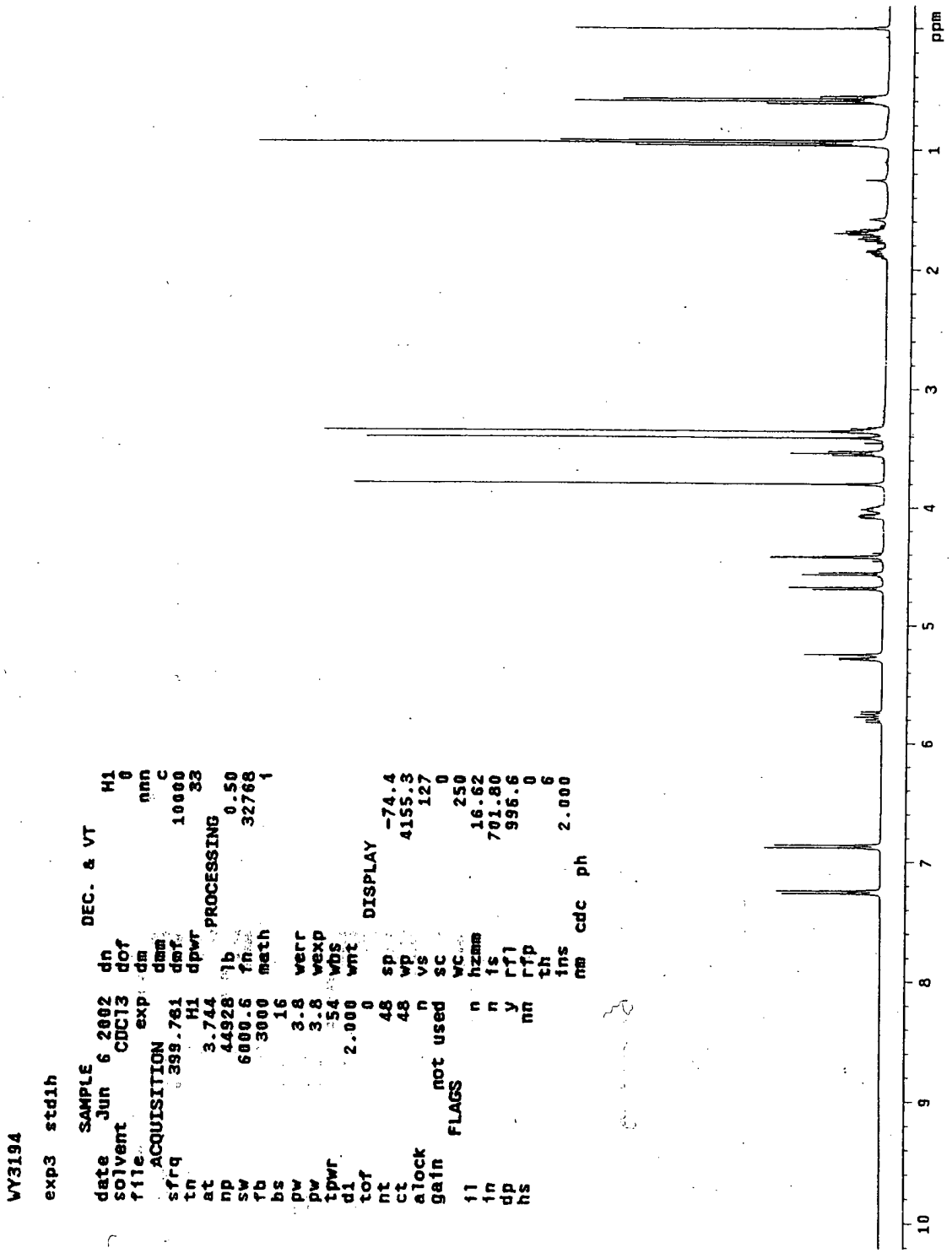

VY3194
exp3 stdih
SAMPLE
date Jun 6 2002
solvent CDCl3
file exp
ACQUISITION
sfrq 399.761
tn H1
at 3.744
np 44928
sw 6000.6
fb 3000
bs 16
pw 3.8
pw 3.8
tpwr 54
d1 2.000
tof 0
nt 48
ct 48
alock n
gain not used
FLAGS
f1 n
in n
dp y
hs nn
DEC. & VT
dn H1
dof 0
dm nnn
dmm c
dmf 10000
dpwr 33
PROCESSING
lb 0.50
fn 32768
math 1
werr
wexp
wbs
wnt
DISPLAY
sp -74.4
wp 4155.3
vs 127
sc 0
wc 250
hzmm 16.62
is 701.80
rfl 996.6
rfp 0
th 6
ins 2.000
nm cdc ph
ppm
1
2
3
4
5
6
7
8
9
10

FIG. 15

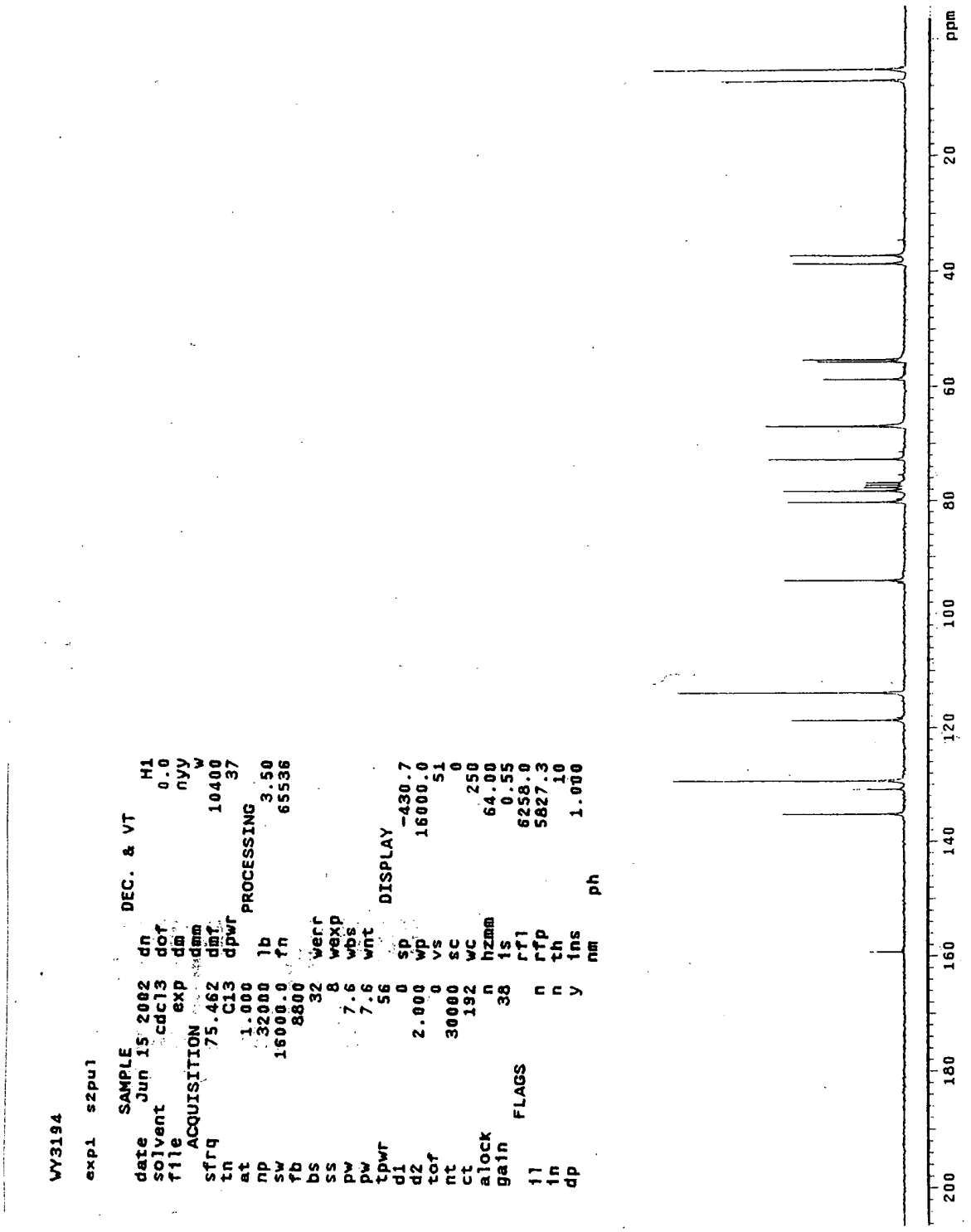

WY3194
expl s2pul
SAMPLE
date Jun 15 2002
solvent cdcl3
file exp
ACQUISITION
sfrq 75.462
tn C13
at 1.000
np 32000
sw 16000.0
fb 8800
bs 32
ss 8
pw 7.6
pw 7.6
tpwr 56
d1 0
d2 2.000
tof 0
nt 30000
ct 192
alock n
gain 38
FLAGS
il n
in n
dp y
DEC. & VT
dn H1
dof 0.0
dm nyy
dmm w
dmf 10400
dpwr 37
PROCESSING
lb 3.50
fn 65536
werr
wexp
wbs
wnt
DISPLAY
sp -430.7
wp 16000.0
vs 51
sc 0
wc 250
hzmm 64.00
is 0.55
rfl 6258.0
rfp 5827.3
th 10
ins 1.000
nm ph
200
180
160
140
120
100
80
60
40
20
ppm

FIG. 16

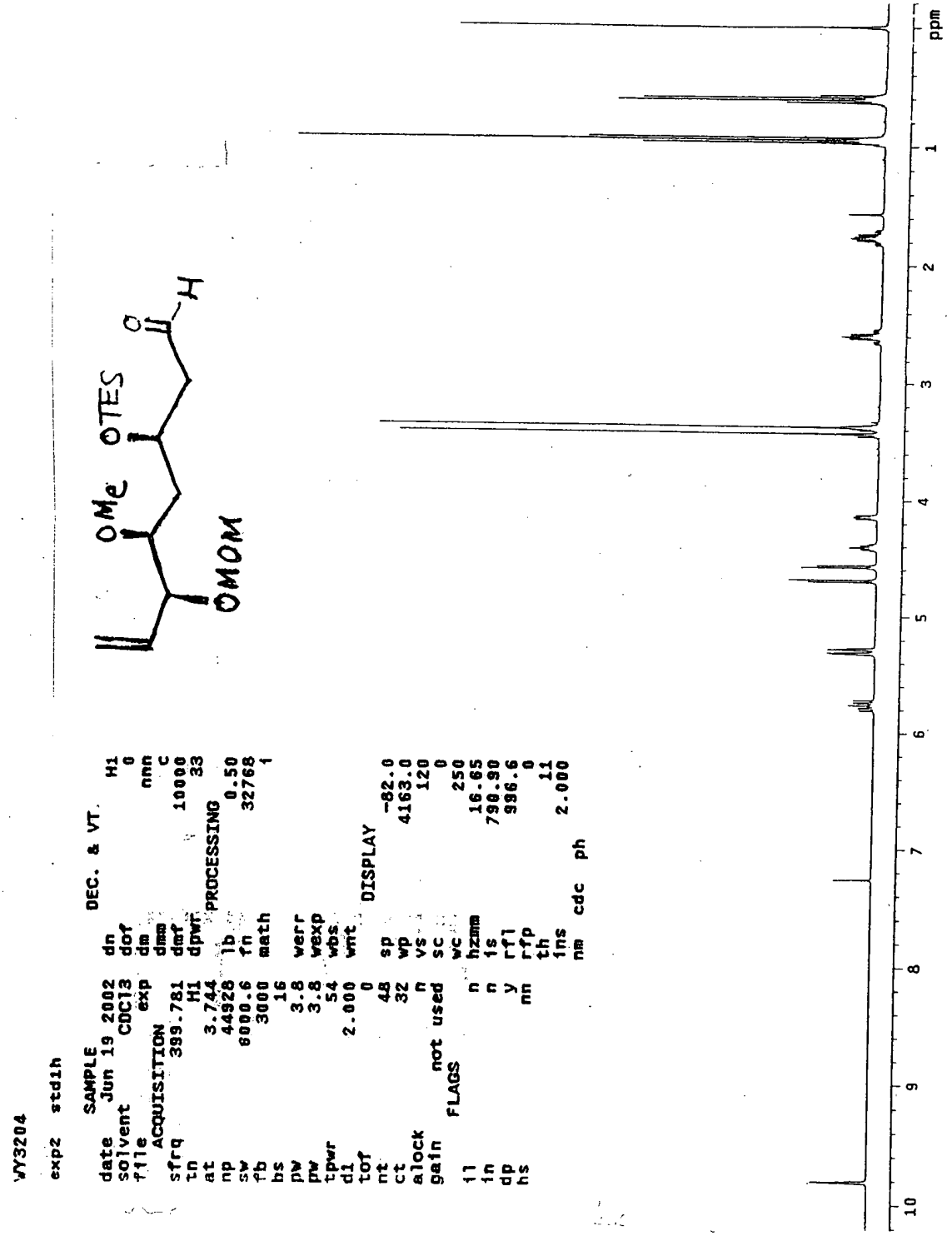

VY3204
exp2 std1h
SAMPLE
date Jun 19 2002
solvent CDCl3
file exp
ACQUISITION
sfrq 399.781
tn H1
at 3.744
np 44928
sw 6000.6
fb 3000
bs 16
pw 3.8
pw 3.8
tpwr 54
d1 2.000
tof 0
nt 48
ct 32
alock n
gain n
FLAGS
not used
fl n
in n
dp y
hs nn
DEC. & VT.
dn H1
dof 0
dm nnn
dmm c
dmf 10000
dpwr 33
PROCESSING
lb 0.50
fn 32768
math f
werr
wexp
wbs
wnt
DISPLAY
sp -82.0
wp 4163.0
vs 120
sc 0
wc 250
hzmm 16.65
is 790.90
rfl 996.6
rfp 0
th 11
ins 2.000
nm cdc ph
OMOM
OMe
OTES
H
O
ppm
1
2
3
4
5
6
7
8
9
10

FIG. 17

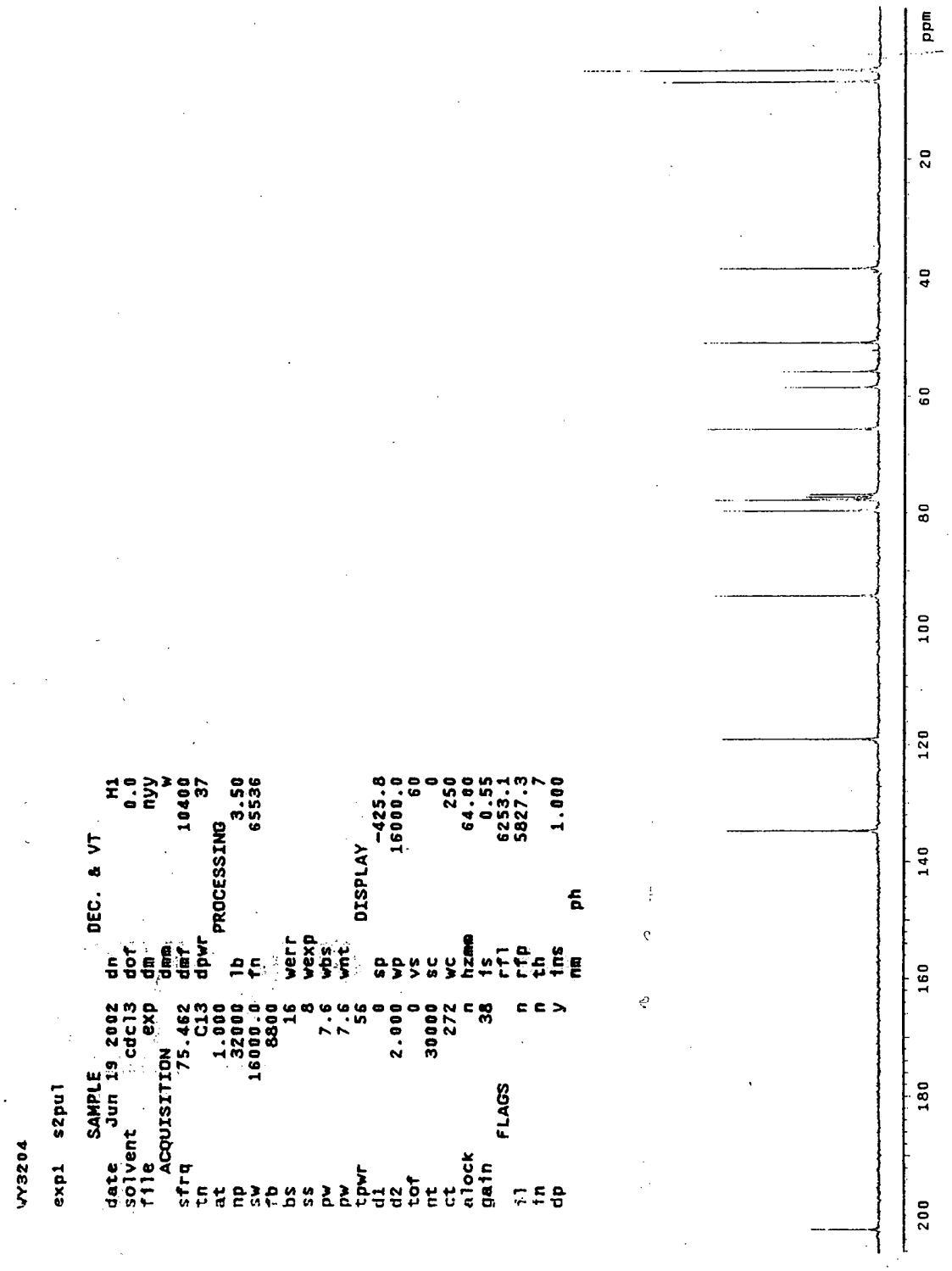

VY3204
exp1 s2pul
SAMPLE
date Jun 19 2002
solvent cdcl3
file exp
ACQUISITION
sfrq 75.462
tn C13
at 1.000
np 32000
sw 16000.0
fb 8800
bs 16
ss 8
pw 7.6
pw 7.6
tpwr 56
d1 0
d2 2.000
tof 0
nt 30000
ct 272
alock n
gain 38
FLAGS
DEC. & VT
dn H1
dof 0.0
dm nyy
dmm w
dmf 10400
dpwr 37
PROCESSING
lb 3.50
fn 65536
werr
wexp
wbs
wnt
DISPLAY
sp -425.8
wp 16000.0
vs 60
sc 0
wc 250
hzmm 64.00
is 0.55
rfl 6253.1
rfp 5827.3
th 7
ins 1.000
ph
nm
ppm
200
180
160
140
120
100
80
60
40
20

FIG. 18

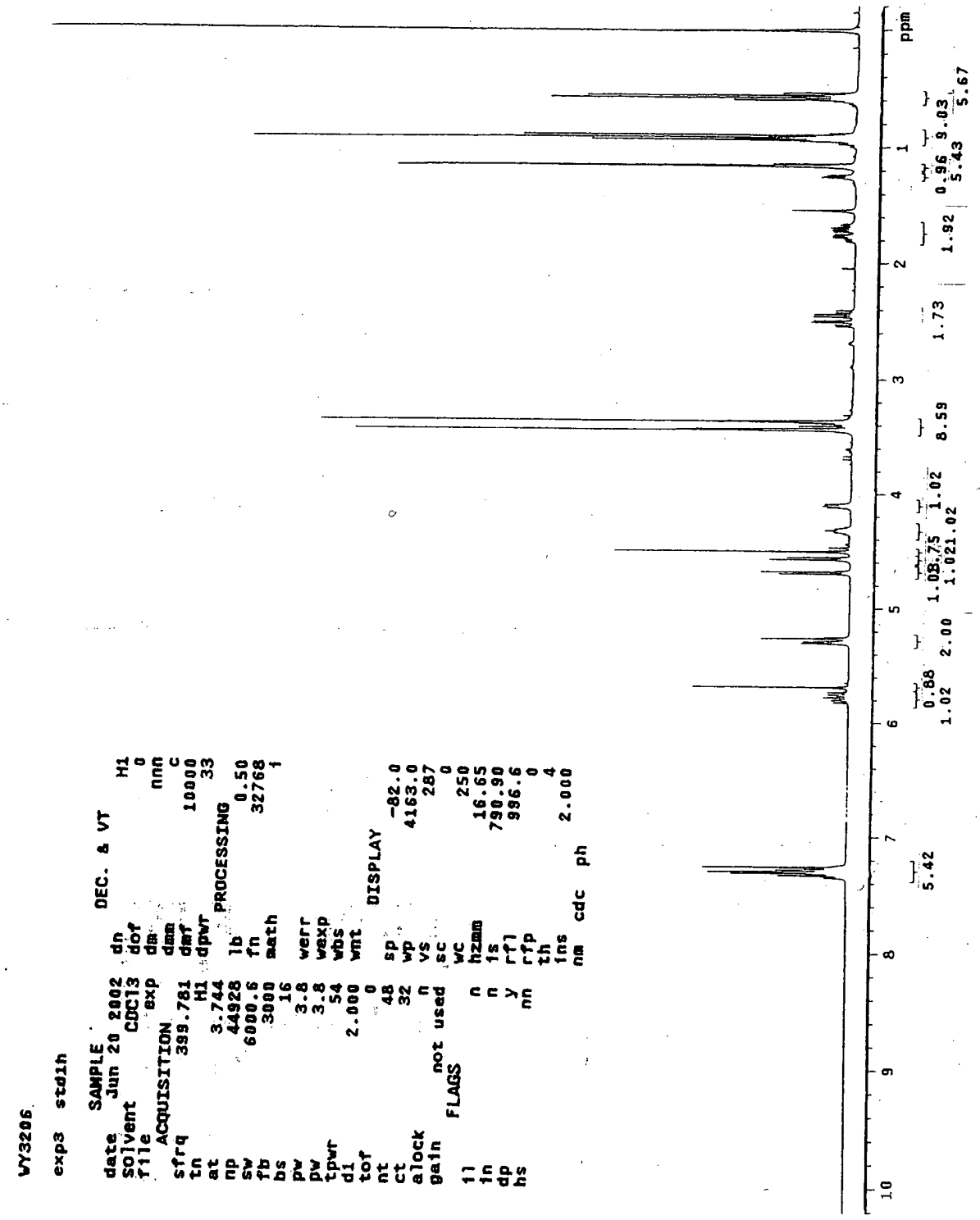

VY3206
exp3 stdih
SAMPLE
date Jun 20 2002
solvent CDCl3
file exp
ACQUISITION
sfrq 399.781
tn H1
at 3.744
np 44928
sw 6000.6
fb 3000
bs 16
pw 3.8
pw 3.8
tpwr 54
d1 2.000
tof 0
nt 48
ct 32
alock n
gain not used
FLAGS
ll n
in n
dp y
hs nn
DEC. & VT
dn H1
dof 0
da nnn
dmm c
dmf 10000
dpwr 33
PROCESSING
lb 0.50
fn 32768
math f
werr
wexp
wbs
wnt
DISPLAY
sp -82.0
wp 4163.0
vs 287
sc 0
wc 250
hzmm 16.65
is 790.90
rfl 996.6
rfp 0
th 4
ins 2.000
nm cdc ph
5.42
0.88
1.02
2.00
1.08.75
1.02
1.021.02
8.59
1.73
1.92
0.96
9.03
5.43
5.67
ppm

FIG. 19

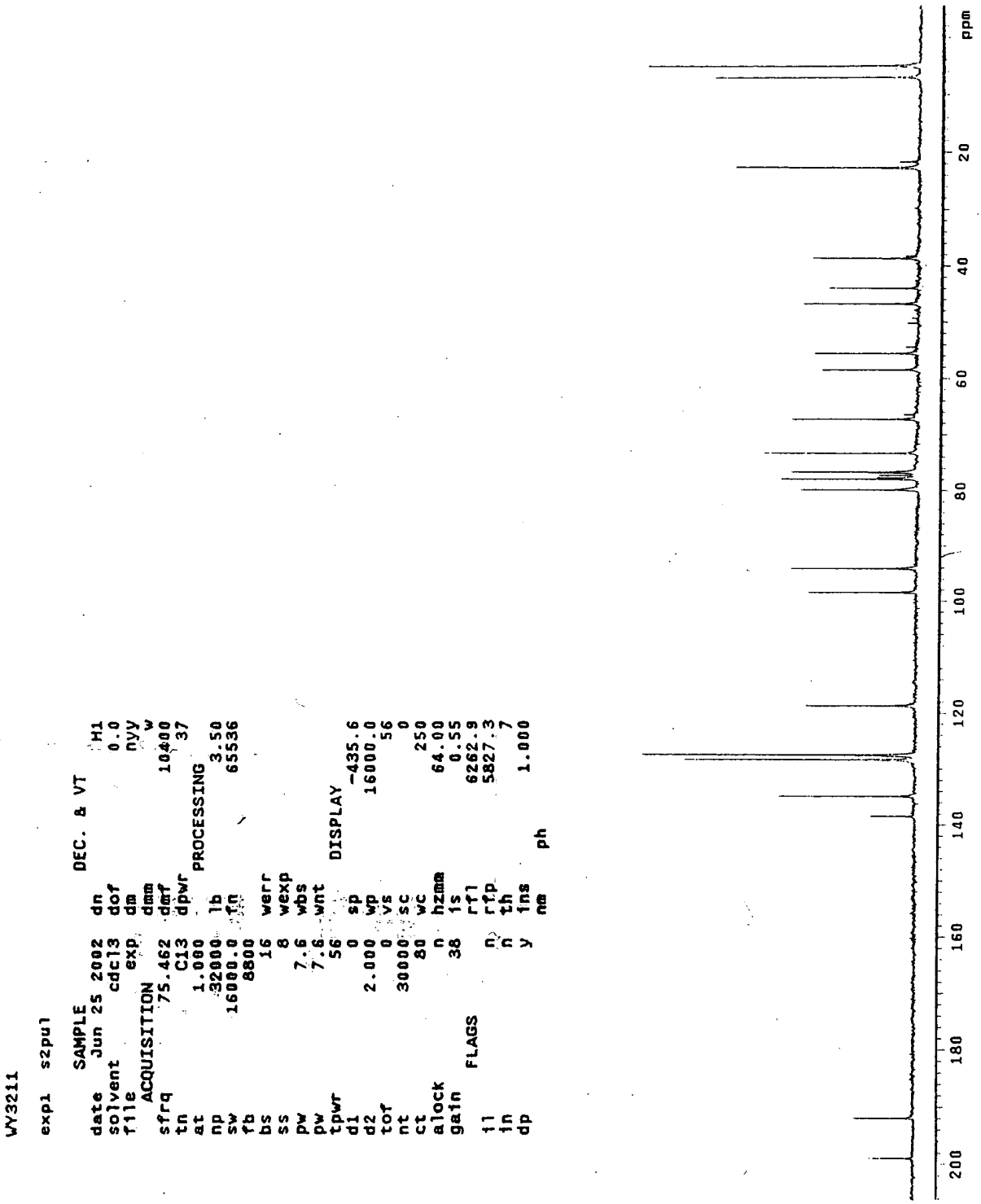

WY3211
expl s2pul
SAMPLE
date Jun 25 2002
solvent cdcl3
file exp
ACQUISITION
sfrq 75.462
tn C13
at 1.000
np 32000
sw 16000.0
fb 8800
bs 16
ss 8
pw 7.6
pw 7.6
tpwr 56
d1 0
d2 2.000
tof 0
nt 30000
ct 80
alock n
gain 38
FLAGS
il n
in n
dp y
DEC. & VT
dn H1
dof 0.0
dm nyy
dmm w
dmf 10400
dpwr 37
PROCESSING
lb 3.50
fn 65536
werr
wexp
wbs
wnt
DISPLAY
sp -435.6
wp 16000.0
vs 56
sc 0
wc 250
hzmm 64.00
is 0.55
rfl 6262.9
rfp 5827.3
th 7
ins 1.000
nm
ph
ppm
200
180
160
140
120
100
80
60
40
20

FIG. 20

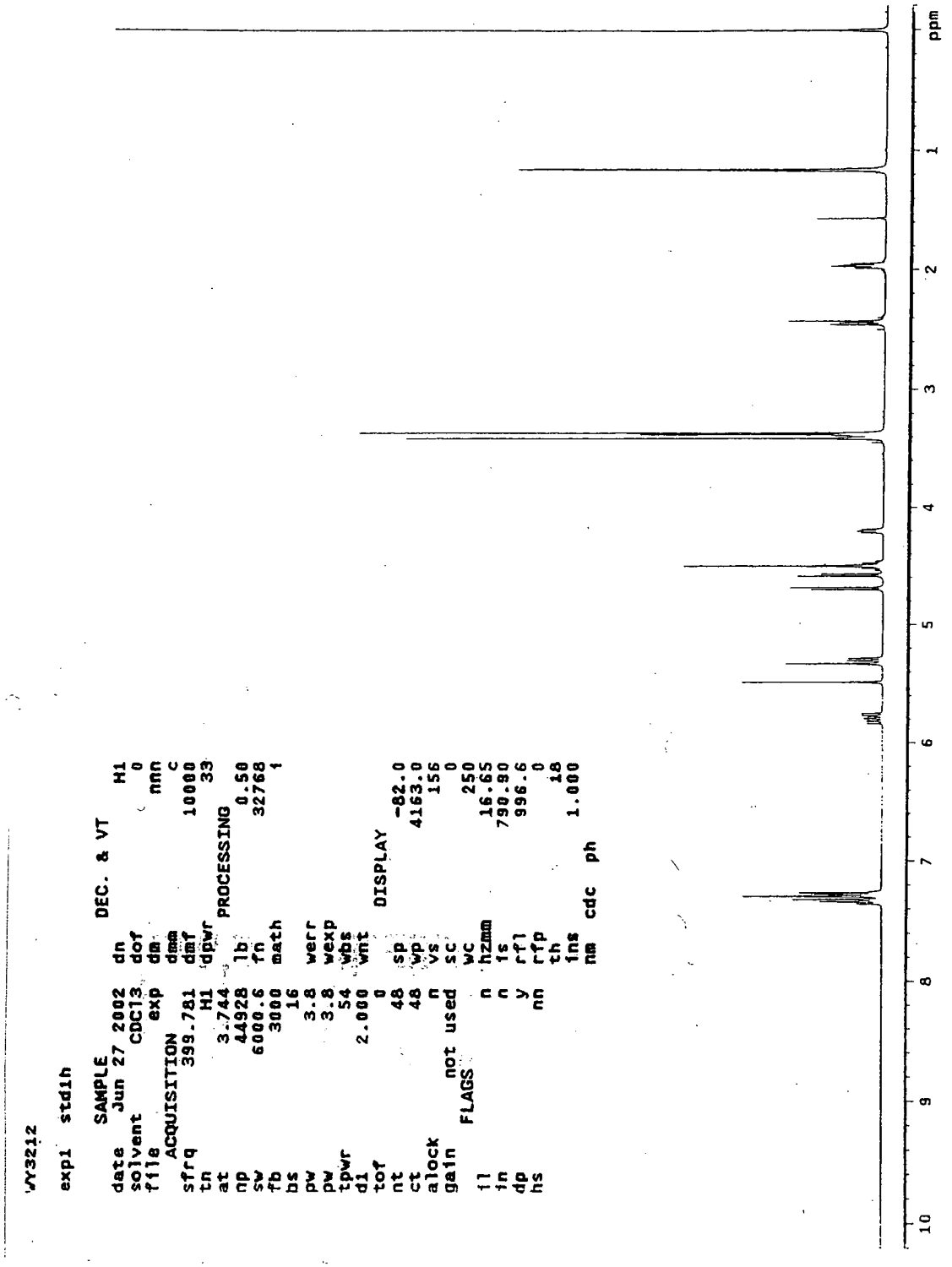

VY3212
expl stdih
SAMPLE
date Jun 27 2002
solvent CDCl3
file
ACQUISITION
sfrq 399.781
tn H1
at 3.744
np 44928
sw 6000.6
fb 3000
bs 16
pw 3.8
pw 3.8
tpwr 54
d1 2.000
tof 0
nt 48
ct 48
alock n
gain not used
FLAGS
fl n
in n
dp y
hs nn
DEC. & VT
dn H1
dof 0
dm nnn
dmm c
dmf 10000
dpwr 33
PROCESSING
lb 0.50
fn 32768
math 1
werr
wexp
wbs
wnt
DISPLAY
sp -82.0
wp 4163.0
vs 156
sc 0
wc 250
hzmm 16.65
is 790.80
rfl 996.6
rfp 0
th 18
ins 1.000
nm cdc ph
ppm
1
2
3
4
5
6
7
8
9
10

FIG. 21

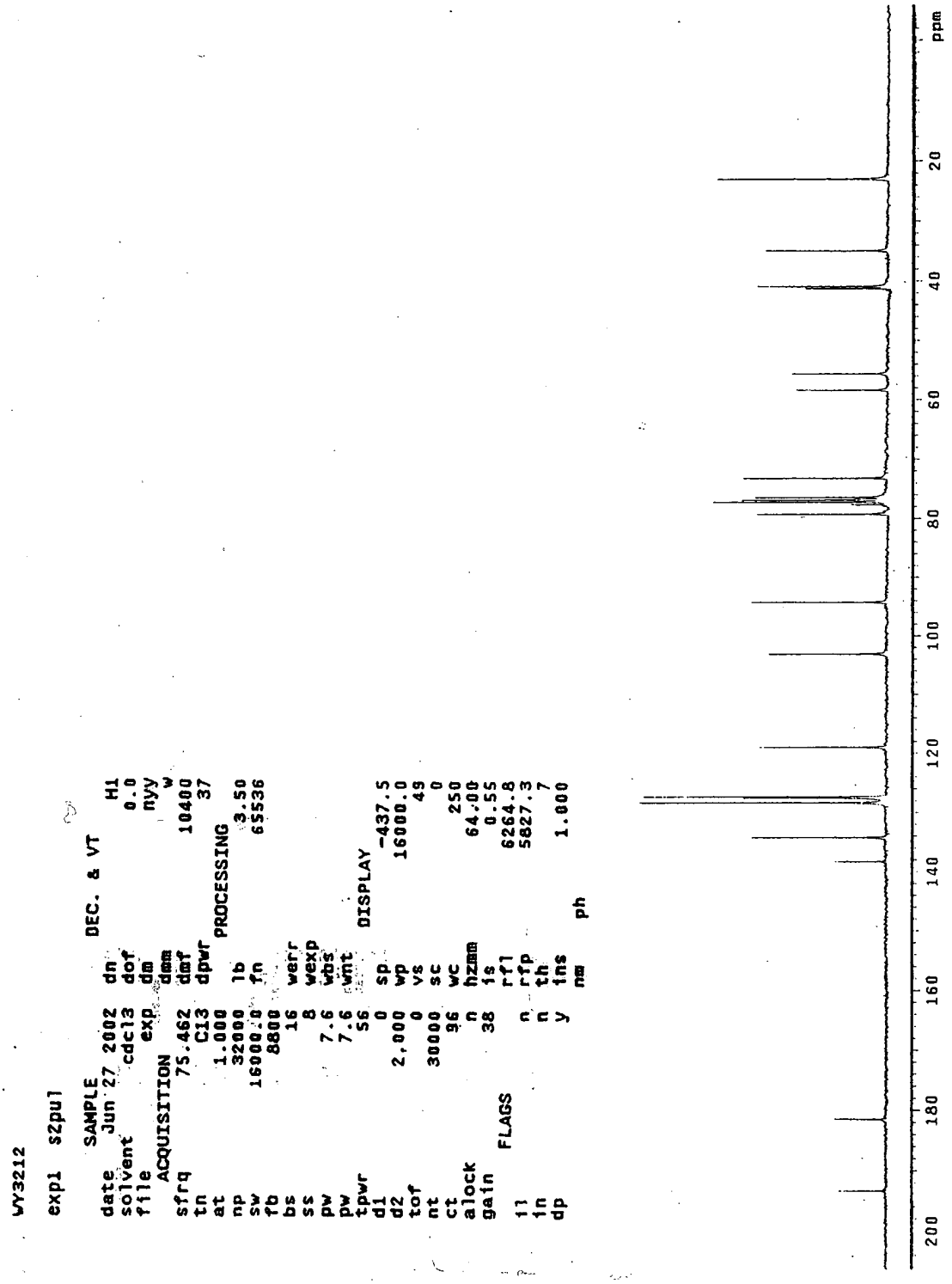

vy3212
expl s2pul
SAMPLE
date Jun 27 2002
solvent cdcl3
file exp
ACQUISITION
sfrq 75.462
tn C13
at 1.000
np 32000
sw 16000.0
fb 8800
bs 16
ss 8
pw 7.6
tpwr 56
d1 0
d2 2.000
tof 0
nt 30000
ct 96
alock n
gain 38
FLAGS
DEC. & VT
dn H1
dof 0.0
dm nyy
dmm w
dmf 10400
dpwr 37
PROCESSING
lb 3.50
fn 65536
werr
wexp
wbs
wnt
DISPLAY
sp -437.5
wp 16000.0
vs 49
sc 0
wc 250
hzmm 64.00
is 0.55
rfl 6264.8
rfp 5827.3
th 7
ins 1.000
ph
200
180
160
140
120
100
80
60
40
20
ppm

FIG. 22

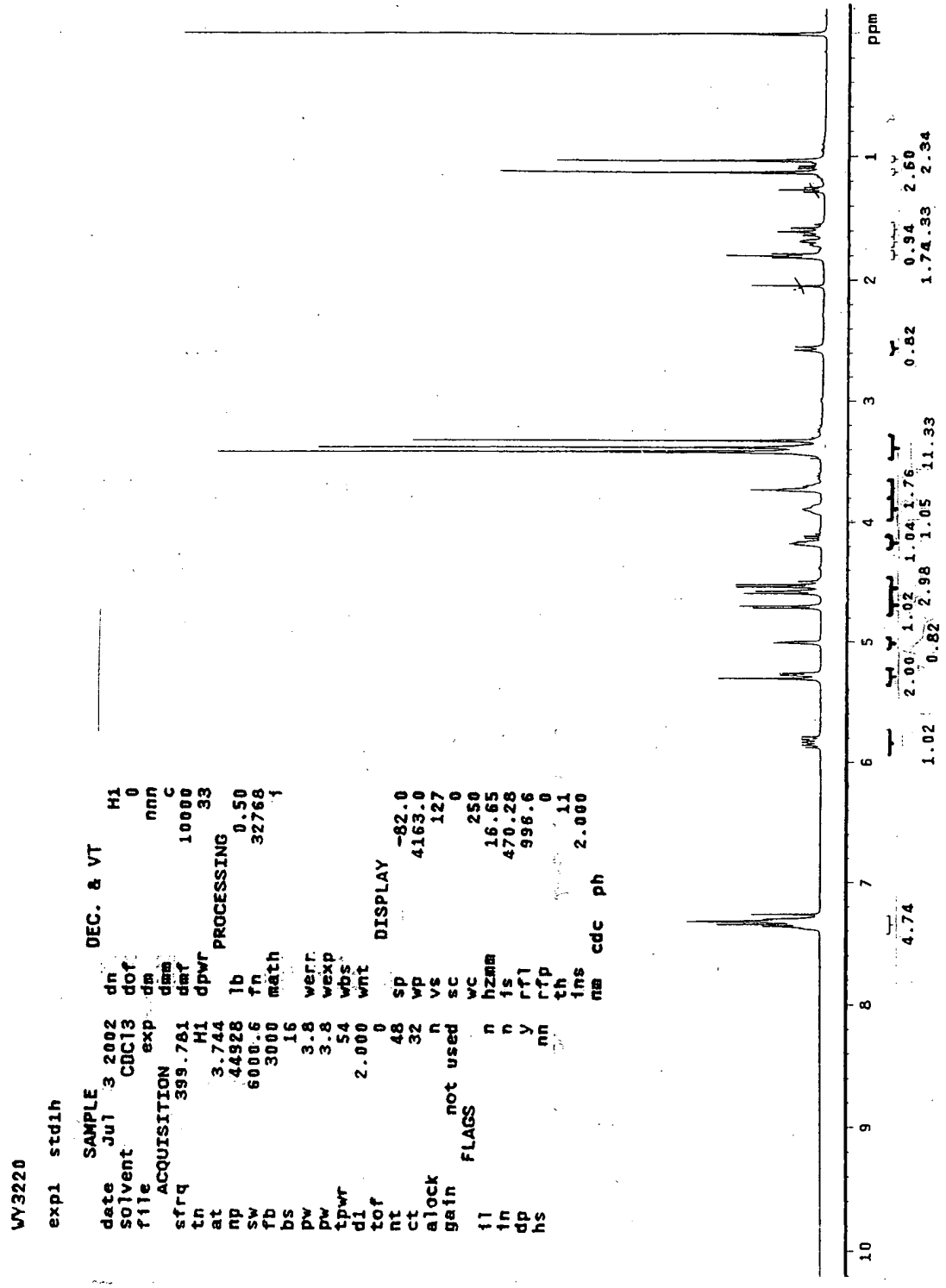

WY3220
expl stdlh
SAMPLE
date Jul 3 2002
solvent CDCl3
file
ACQUISITION
sfrq 399.781
tn H1
at 3.744
np 44928
sw 6000.6
fb 3000
bs 16
pw 3.8
pw 3.8
tpwr 54
d1 2.000
tof 0
nt 48
ct 32
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DEC. & VT
dn H1
dof 0
dm nnn
dmm c
dmf 10000
dpwr 33
PROCESSING
lb 0.50
fn 32768
math f
werr
wexp
wbs
wnt
DISPLAY
sc 0
wc 250
hzmm 16.65
is 470.28
rfl 998.6
rfp 0
th 11
ins 2.000
nm cdc ph
ppm
4.74
1.02
2.00
1.02
0.82
2.98
1.04
1.05
1.76
11.33
0.82
0.94
1.74
2.60
2.34

FIG. 23

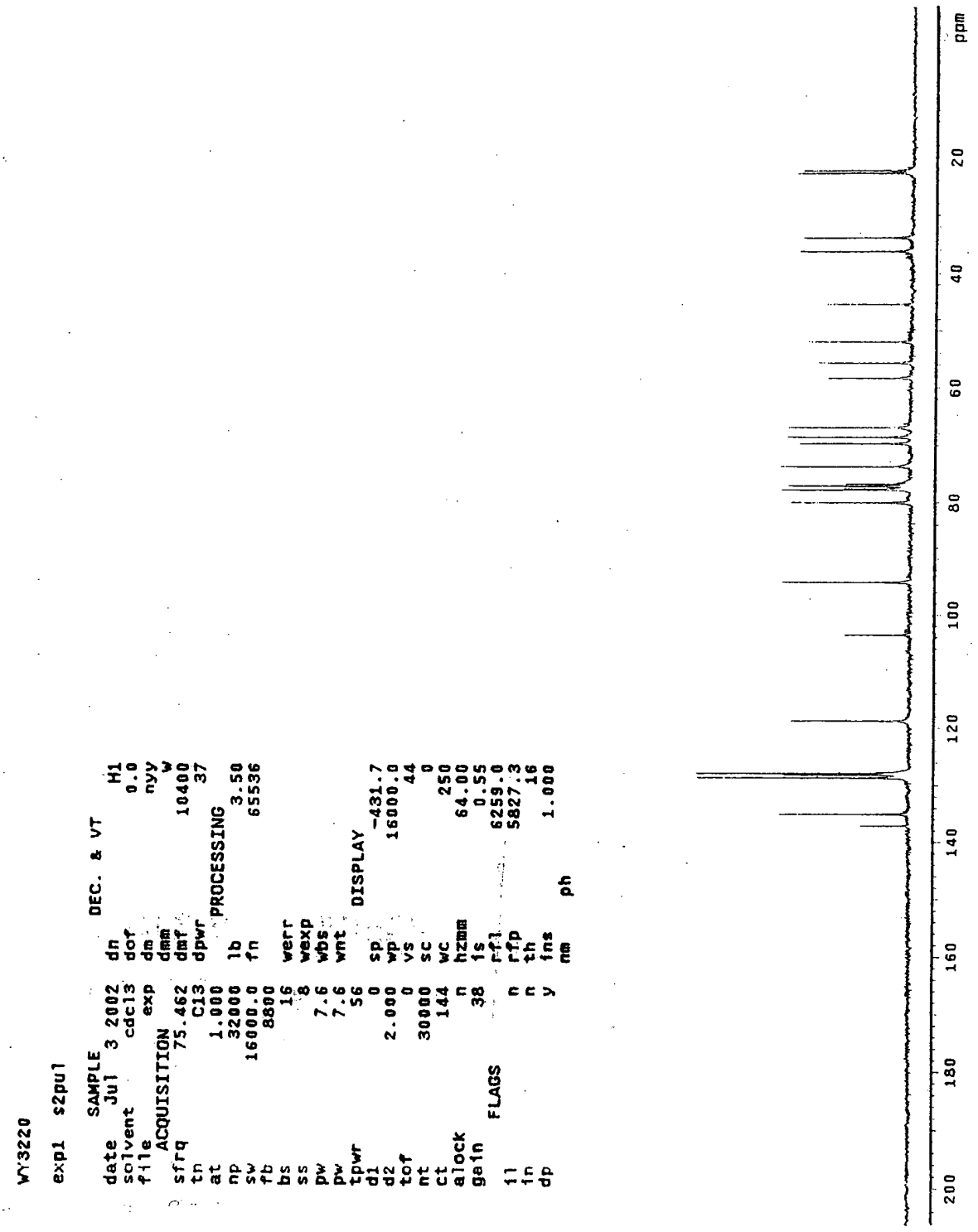

WY3220
expl s2pul
SAMPLE
date Jul 3 2002
solvent cdcl3
file exp
ACQUISITION
sfrq 75.462
tn C13
at 1.000
np 32000
sw 16000.0
fb 8800
bs 16
ss 8
pw 7.6
pw 7.6
tpwr 56
d1 0
d2 2.000
tof 0
nt 30000
ct 144
alock n
gain 38
FLAGS
il n
in n
dp y
DEC. & VT
dn H1
dof 0.0
dm nyy
dmm w
dmf 10400
dpwr 37
PROCESSING
lb 3.50
fn 65536
werr
wexp
wbs
wnt
DISPLAY
sp -431.7
wp 16000.0
vs 44
sc 0
wc 250
hzmm 64.00
is 0.55
rfl 6259.0
rfp 5827.3
th 16
ins 1.000
nm ph
200
180
160
140
120
100
80
60
40
20
ppm

FIG. 24

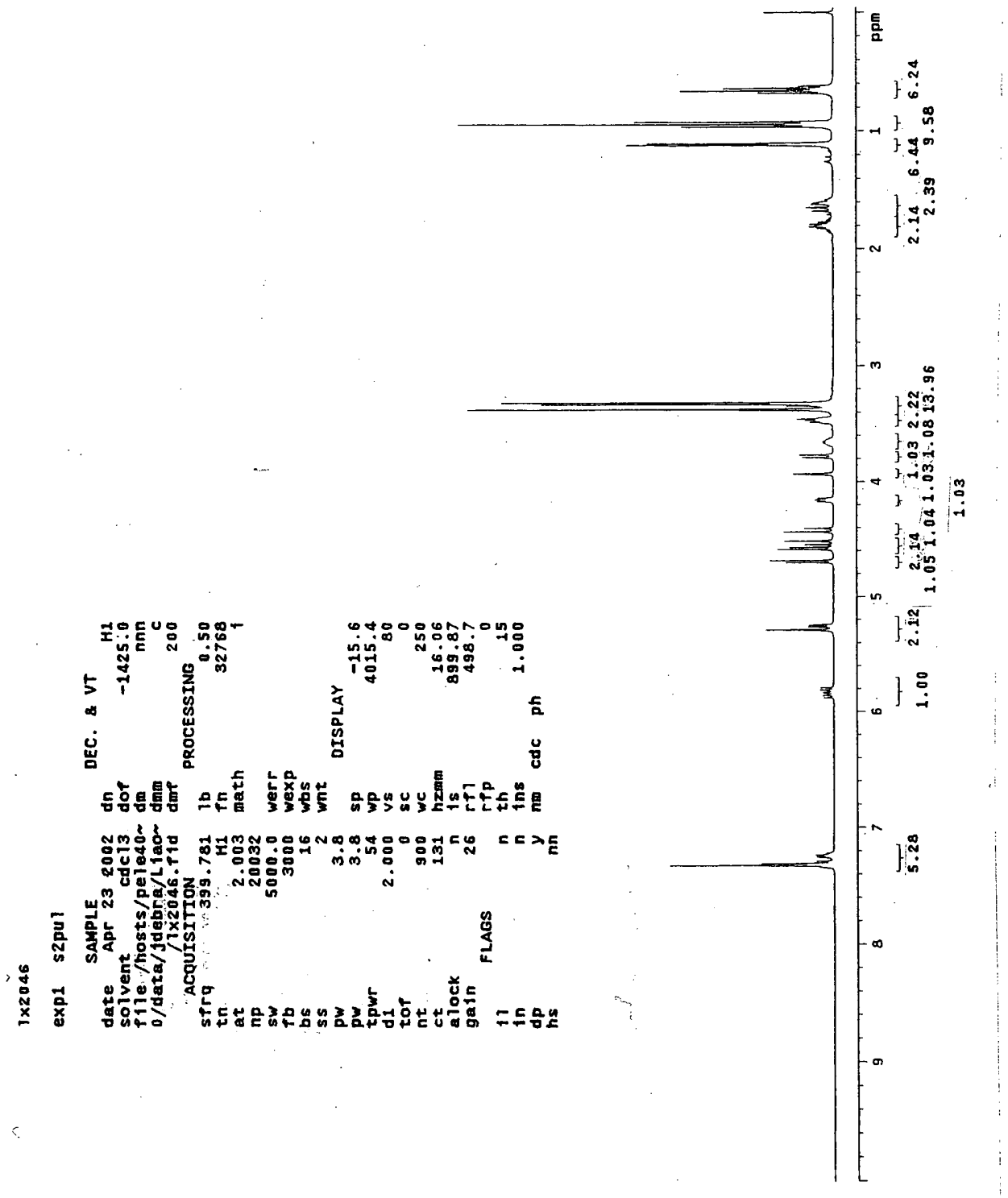

1x2046
exp1 s2pul
SAMPLE
date Apr 23 2002
solvent cdcl3
file /hosts/pele40~
0/data/Jdebra/Liao~
/1x2046.fid
ACQUISITION
sfrq 399.781
tn H1
at 2.003
np 20032
sw 5000.0
fb 3000
bs 16
ss 2
pw 3.8
pw 3.8
tpwr 54
d1 2.000
tof 0
nt 900
ct 131
alock n
gain 26
FLAGS
il n
in n
dp y
hs nn
DEC. & VT
dn H1
dof -1425.0
dm nnn
dmm c
dmf 200
PROCESSING
lb 0.50
fn 32768
math 1
werr
wexp
wbs
wnt
DISPLAY
sp -15.6
wp 4015.4
vs 80
sc 0
wc 250
hzmm 16.06
is 899.87
rfl 498.7
rfp 0
th 15
ins 1.000
ph
cdc
mc
ppm
5.28
1.00
2.12
2.14
1.05
1.04
1.03
1.03
2.22
1.08
13.96
1.03
2.14
2.39
6.44
9.58
6.24

FIG. 25

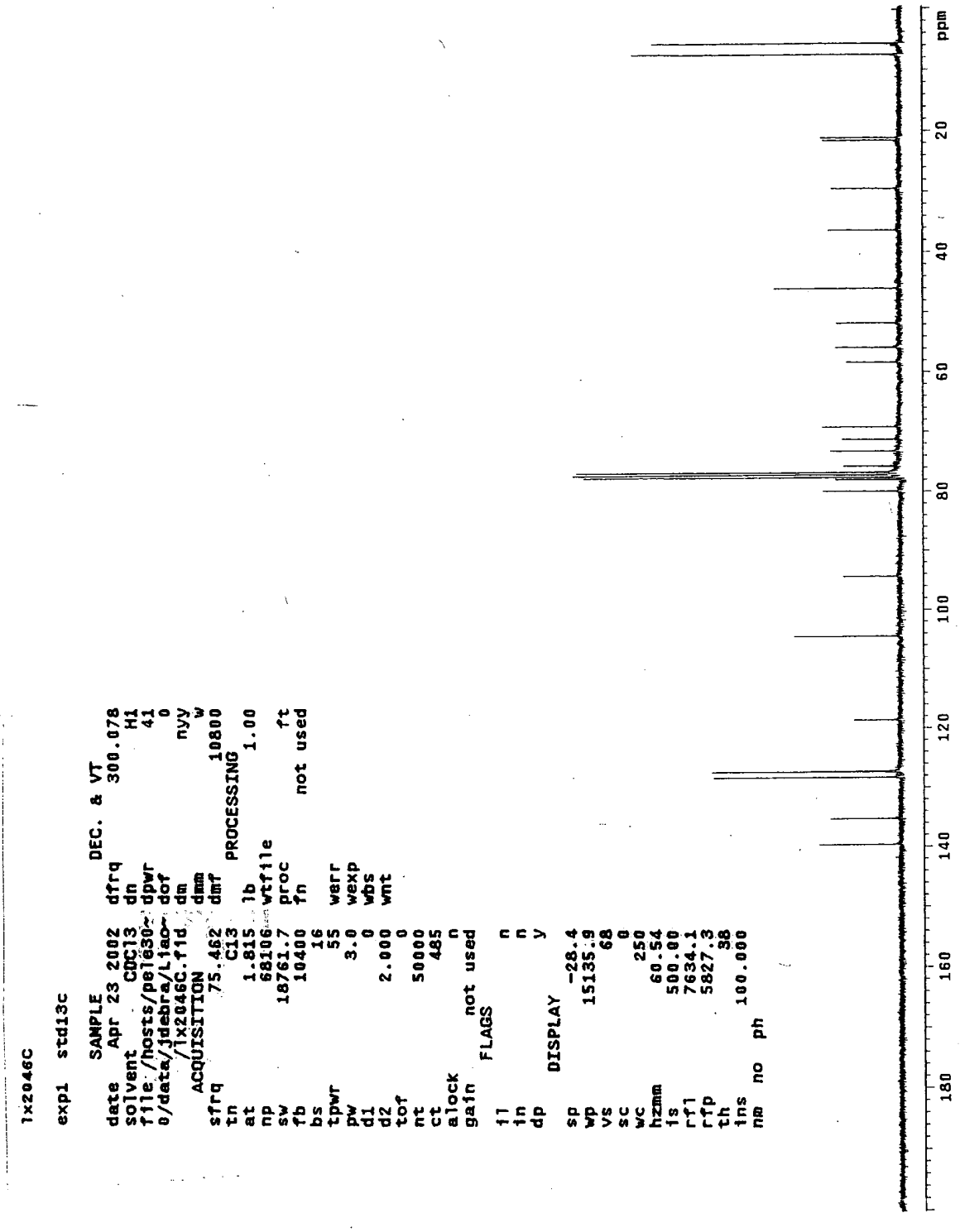

1x2046C
expl std13c
SAMPLE DEC. & VT
date Apr 23 2002 dfrq 300.078
solvent CDCl3 dn H1
file /hosts/pel630~ dpwr 41
0/data/jdebra/Liao~ dof 0
/1x2046C.fid dm nyy
ACQUISITION dmm w
sfrq 75.462 dmf 10800
tn C13 PROCESSING
at 1.815 lb 1.00
np 68106 wtfile
sw 18761.7 proc ft
fb 10400 fn not used
bs 16
tpwr 55 werr
pw 3.0 wexp
d1 0 wbs
d2 2.000 wnt
tof 0
nt 50000
ct 485
alock n
gain not used
FLAGS
f1 n
in n
dp y
DISPLAY
sp -28.4
wp 15135.9
vs 68
sc 0
wc 250
hzmm 60.54
is 500.00
rf1 7634.1
rfp 5827.3
th 38
ins 100.000
nm no ph
180 160 140 120 100 80 60 40 20 ppm

FIG. 26

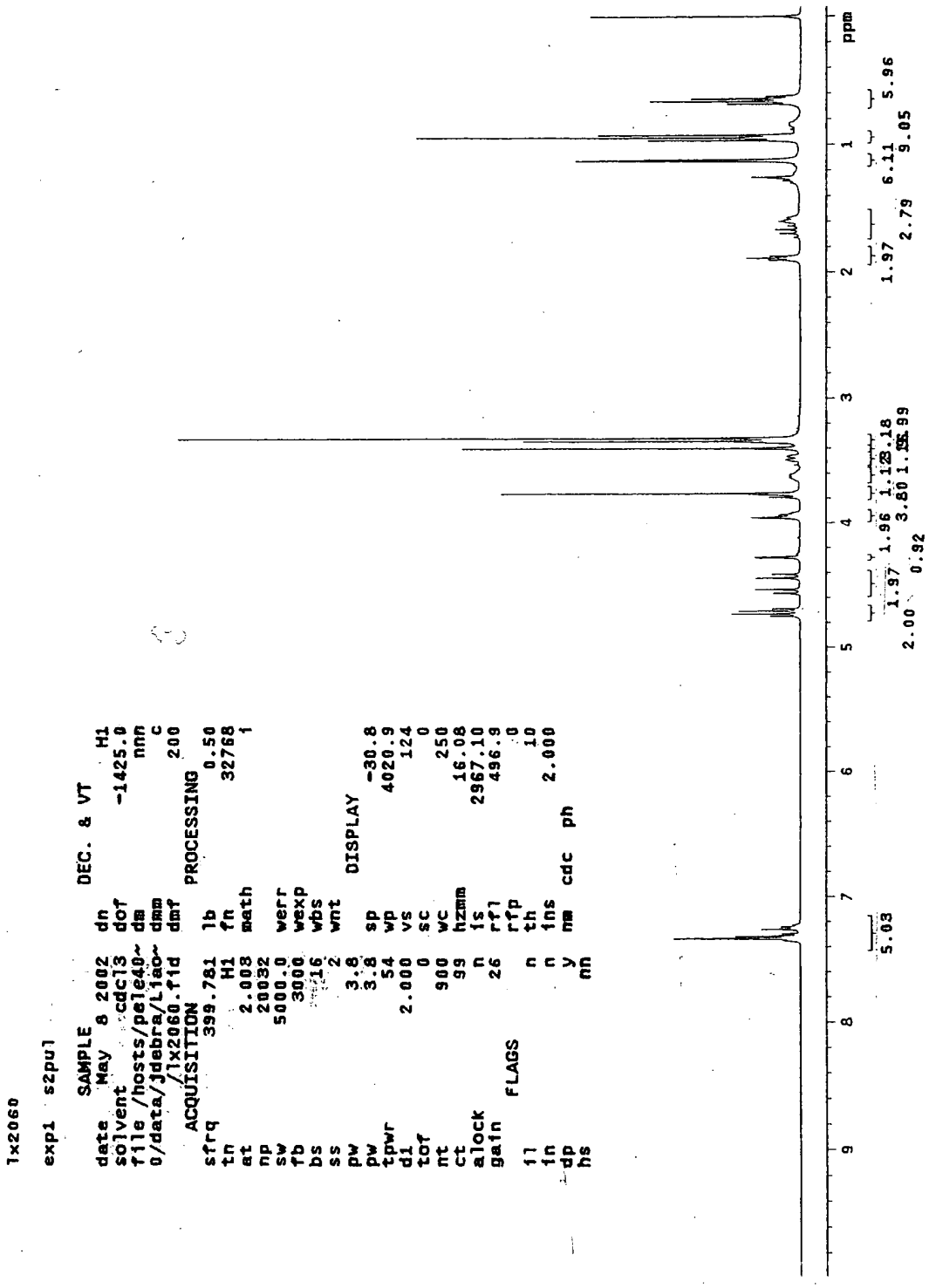

1x2060
exp1 s2pul
SAMPLE
date May 8 2002
solvent cdcl3
file /hosts/pele40~
0/data/jdebra/Liao~
/1x2060.fid
ACQUISITION
sfrq 399.781
tn H1
at 2.003
np 20032
sw 5000.0
fb 3000
bs 16
ss 2
pw 3.8
pw 3.8
tpwr 54
d1 2.000
tof 0
nt 900
ct 99
alock n
gain 26
FLAGS
DEC. & VT
dn H1
dof -1425.0
dm nnn
dmm c
dmf 200
PROCESSING
lb 0.50
fn 32768
math 1
werr
wexp
wbs
wnt
DISPLAY
sp -30.8
wp 4020.9
vs 124
sc 0
wc 250
hzmm 16.08
is 2967.10
rfl 496.9
rfp 0
th 10
2.000
ins
nm cdc ph
ppm
5.03
2.00
1.97
0.92
1.96
3.80
2.79
1.97
6.11
9.05
5.96

FIG. 27

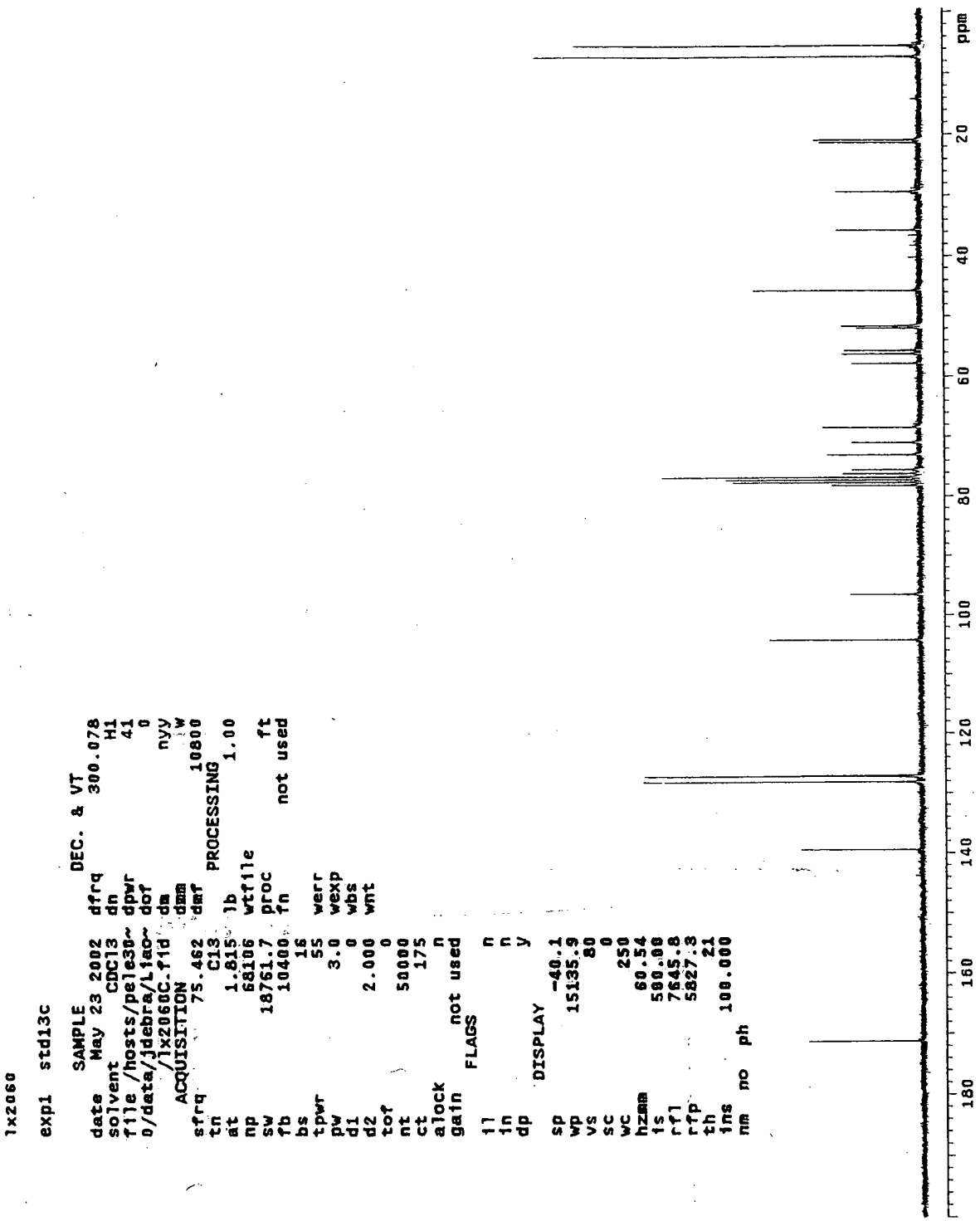

1x2060
expl std13c
SAMPLE DEC. & VT
date May 23 2002 dfrq 300.078
solvent CDCl3 dn H1
file /hosts/pele30~ dpwr 41
d/data/jdebra/L1ac~ dof 0
/1x2060C.fid dm nyy
ACQUISITION dmm w
sfrq 75.462 dmf 10800
tn C13 PROCESSING
at 1.815 lb 1.00
np 68106 wtfile
sw 18761.7 proc ft
fb 10400 fn not used
bs 16
tpwr 55 werr
pw 3.0 wexp
d1 0 wbs
d2 2.000 wnt
tof 0
nt 50000
ct 175
alock n
gain not used
FLAGS
ll n
in n
dp y
DISPLAY
sp -40.1
wp 15135.9
vs 80
sc 0
wc 250
hzmm 60.54
is 500.00
rfl 7645.8
rfp 5827.3
th 21
ins 100.000
nm no ph
180 160 140 120 100 80 60 40 20 ppm

FIG. 28

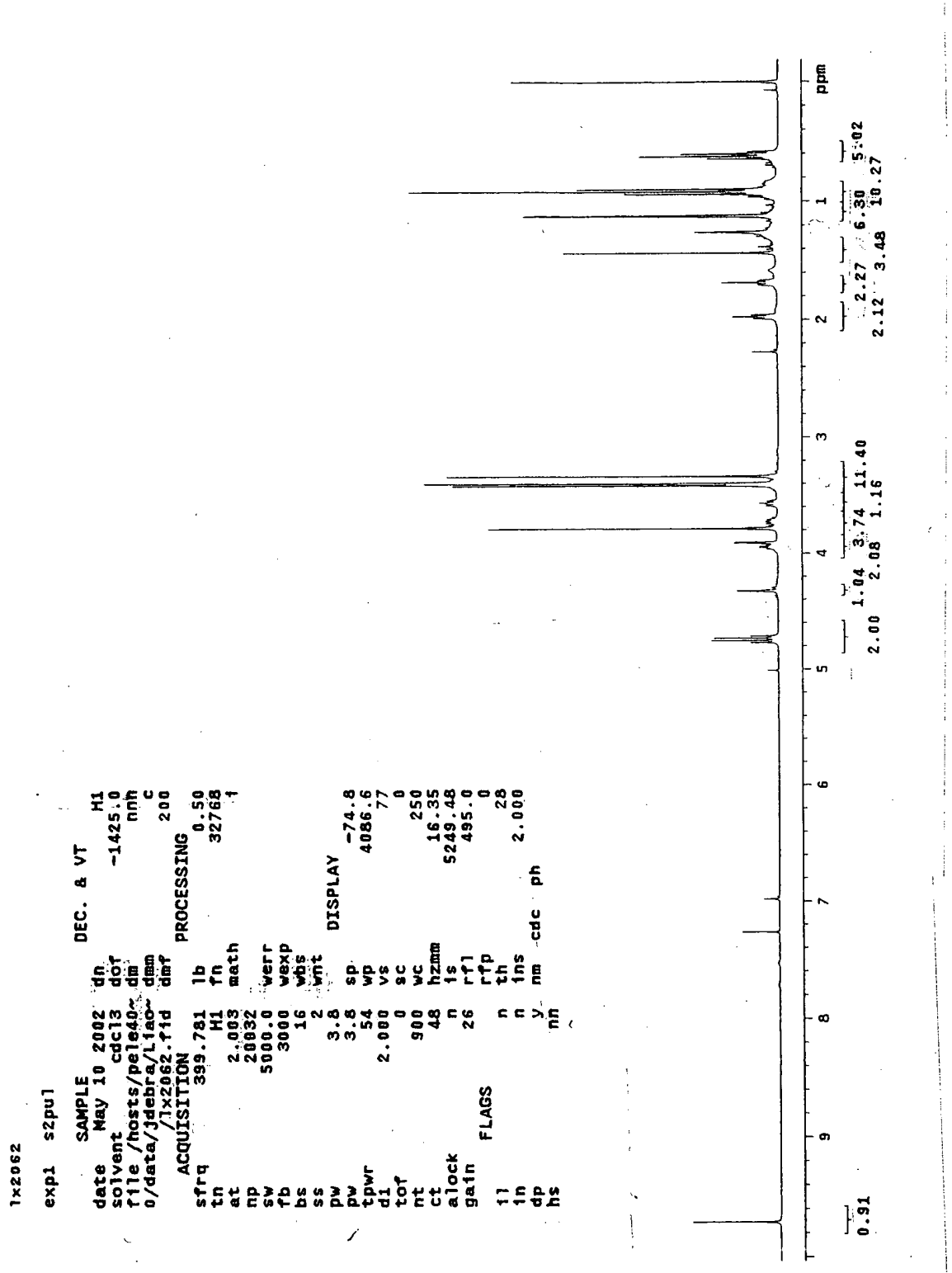

1x2062
expl s2pul
SAMPLE
date May 10 2002
solvent cdcl3
file /hosts/pele40~/dm
o/data/jdebra/Liao~/dmm
/1x2062.fid dmf
ACQUISITION
sfrq 399.781 lb 0.50
tn H1 fn 32768
at 2.003 math
np 20832
sw 5000.0 werr
fb 3000 wexp
bs 16 wbs
ss 2 wnt
pw 3.8 DISPLAY
pw 3.8 sp -74.8
tpwr 54 wp 4086.6
d1 2.000 vs 77
tof 0 sc 0
nt 900 wc 250
ct 48 hzmm 16.35
alock n is 5249.48
gain 26 rfl 495.0
FLAGS rfp 0
th 28
il n n ins 2.000
in n y nm cdc ph
dp y
hs nn
DEC. & VT
dn H1
dof -1425.0
dm nnh
dmm c
dmf 200
PROCESSING
ppm
0.91
2.00 2.08 1.16
1.04 3.74 11.40
2.12 3.48 10.27
2.27 6.30 5.02

FIG.29

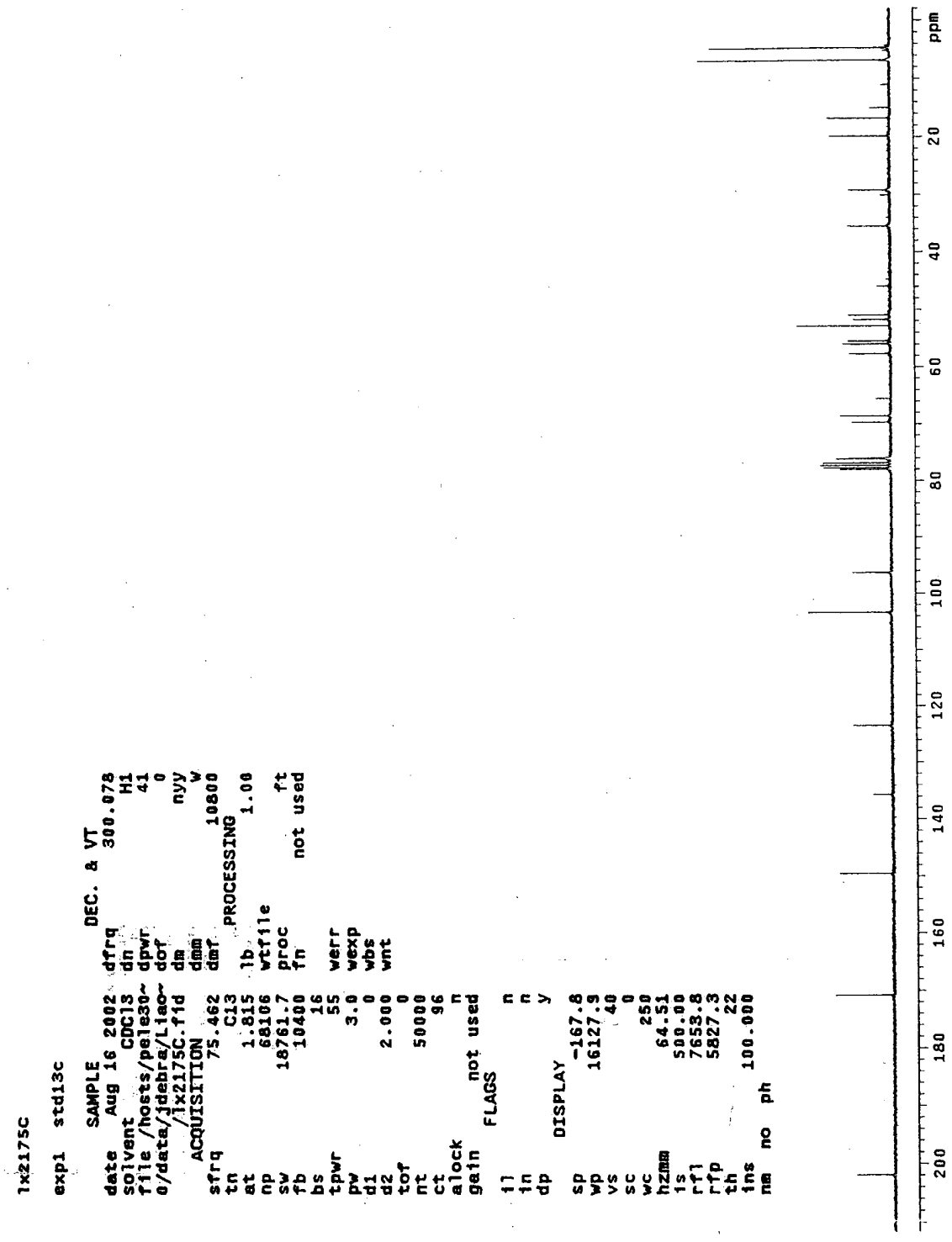

1x2175C
expl std13c
SAMPLE DEC. & VT
date Aug 16 2002 dfrq 300.078
solvent CDCl3 dn H1
file /hosts/pele30~ dpwr 41
0/data/jdebra/Liao~ dof 0
/1x2175C.fid dm nyy
ACQUISITION dmm w
sfrq 75.462 dmf 10800
tn C13 PROCESSING
at 1.815 lb 1.00
np 68106 wtfile
sw 18761.7 proc ft
fb 10400 fn not used
bs 16
tpwr 55 werr
pw 3.0 wexp
d1 0 wbs
d2 2.000 wnt
tof 0
nt 50000
ct 96
alock n
gain not used
FLAGS
fl n
in n
dp y
DISPLAY
sp -167.8
wp 16127.9
vs 40
sc 0
wc 250
hzmm 64.51
is 500.00
rfl 7653.8
rfp 5827.3
th 22
ins 100.000
nm no ph
200
180
160
140
120
100
80
60
40
20
ppm

FIG. 30

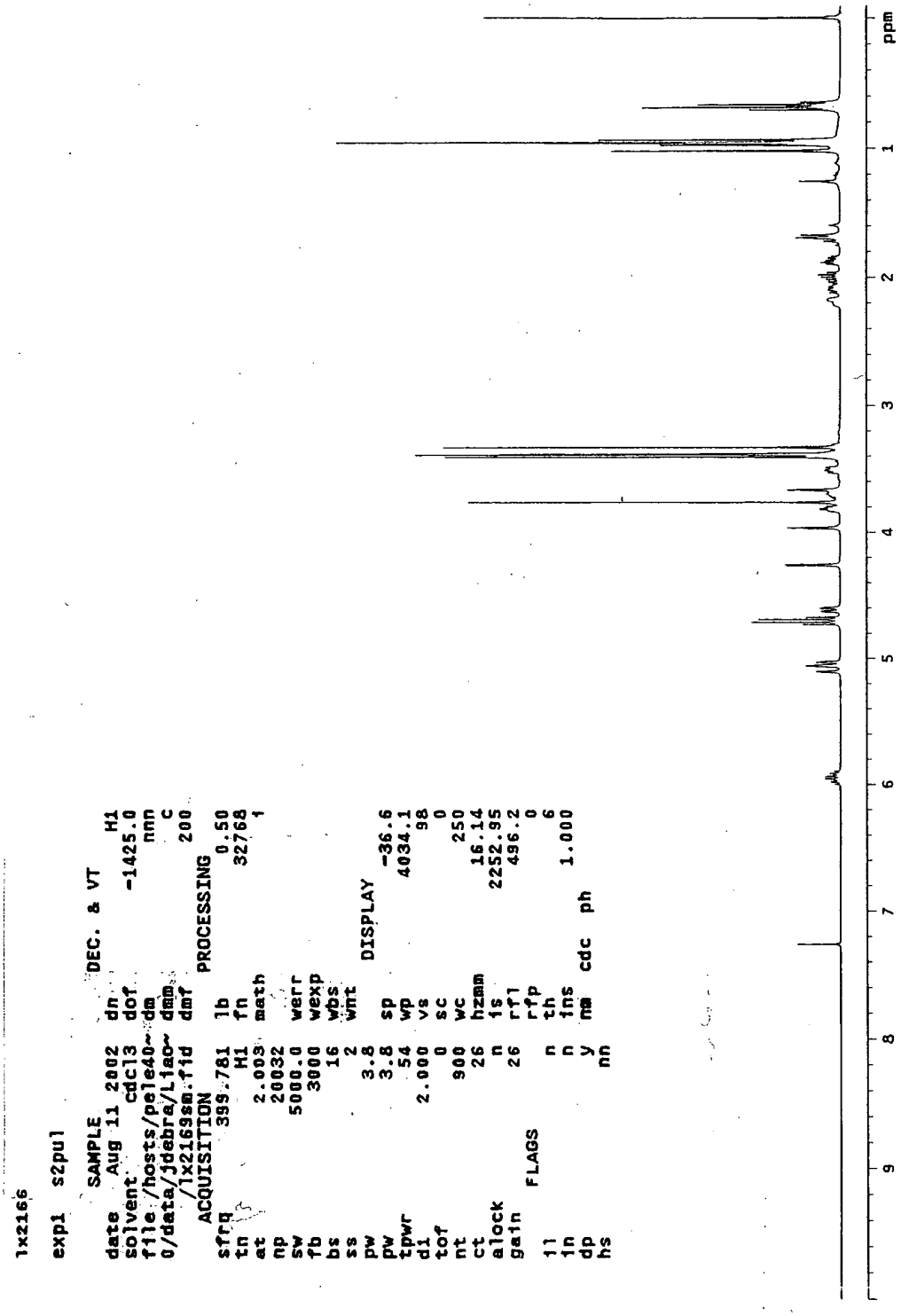

1x2166
expl s2pul
SAMPLE
date Aug 11 2002
solvent cdcl3
file /hosts/pele40~/dm
0/data/jdebra/Liao~/dmm
/1x2169sm.fid dmf
ACQUISITION
sfrq 399.781
tn H1
at 2.003
np 20032
sw 5000.0
fb 3000
bs 16
ss 2
pw 3.8
pw 3.8
tpwr 54
d1 2.000
tof 0
nt 900
ct 26
alock n
gain 26
FLAGS
il n
in n
dp y
hs nn
DEC. & VT
dn H1
dof -1425.0
dm nnn
dmm c
dmf 200
PROCESSING
lb 0.50
fn 32768
math 1
werr
wexp
wbs
wnt
DISPLAY
sp -36.6
wp 4034.1
vs 98
sc 0
wc 250
hzmm 16.14
is 2252.95
rfl 496.2
rfp 0
th 6
ins 1.000
ma cdc ph
ppm

FIG. 31

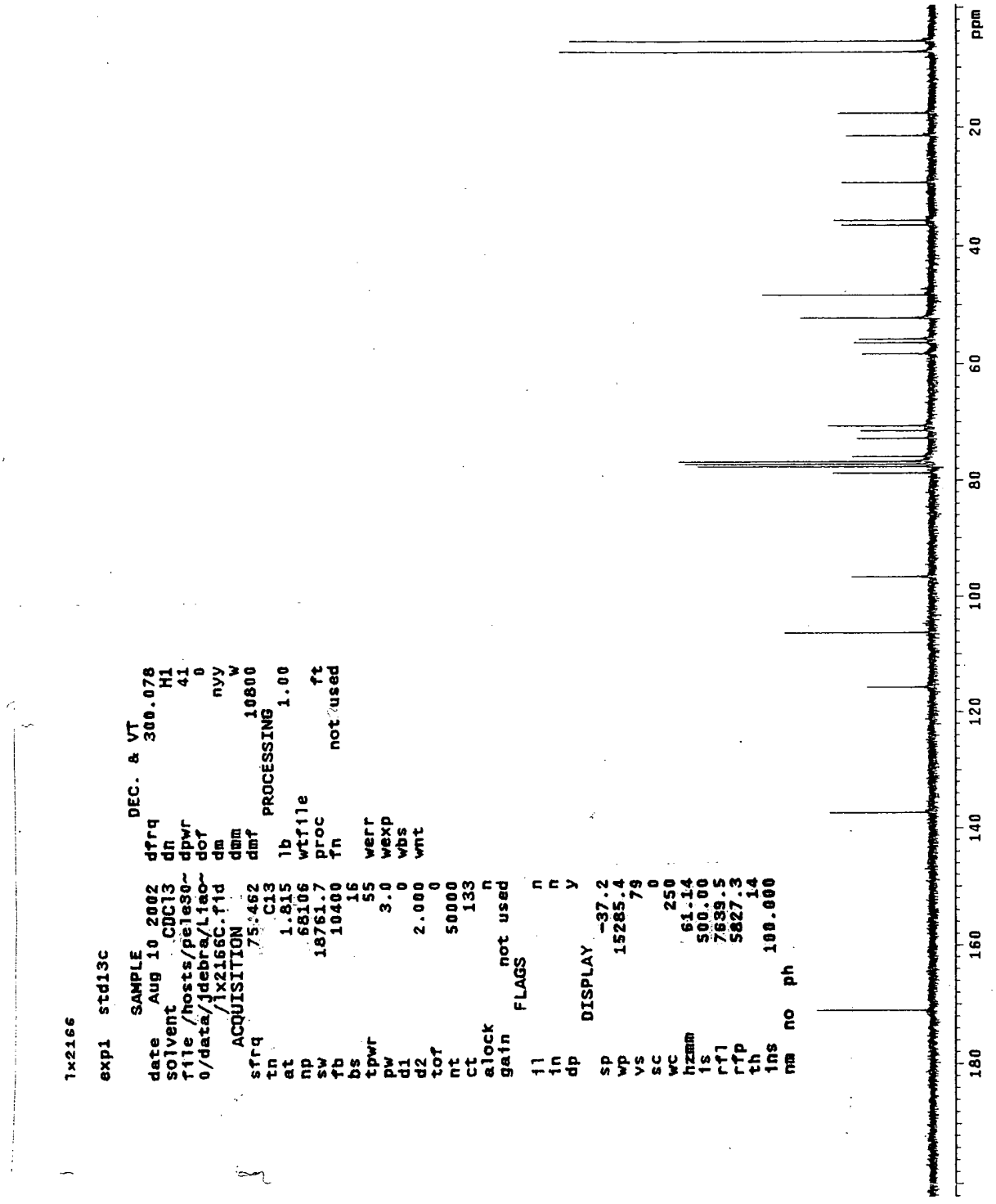

1x2166
exp1 std13c
SAMPLE
date Aug 10 2002
solvent CDCl3
file /hosts/pele30~
0/data/jdebra/Liao~
/1x2166C.fid
ACQUISITION
sfrq 75.462
tn C13
at 1.815
np 68106
sw 18761.7
fb 10400
bs 16
tpwr 55
pw 3.0
d1 0
d2 2.000
tof 0
nt 50000
ct 133
alock n
gain not used
FLAGS
fl n
in n
dp y
DISPLAY
sp -37.2
wp 15285.4
vs 79
sc 0
wc 250
hzmm 61.14
is 500.00
rfl 7639.5
rfp 5827.3
th 14
ins 100.000
nm no ph
DEC. & VT
dfrq 300.078
dn H1
dpwr 41
dof 0
dm nyy
dmm w
dmf 10800
PROCESSING
lb 1.00
wtfile
proc ft
fn not used
werr
wexp
wbs
wnt
ppm
20
40
60
80
100
120
140
160
180

FIG. 32

24
400 MHz
$CDCl_3$

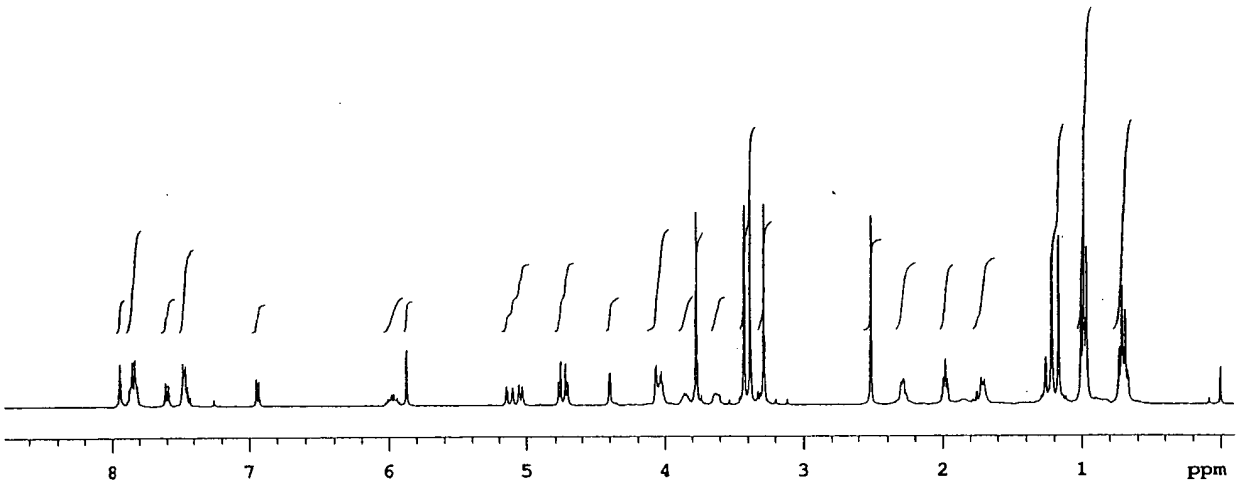


FIG. 33

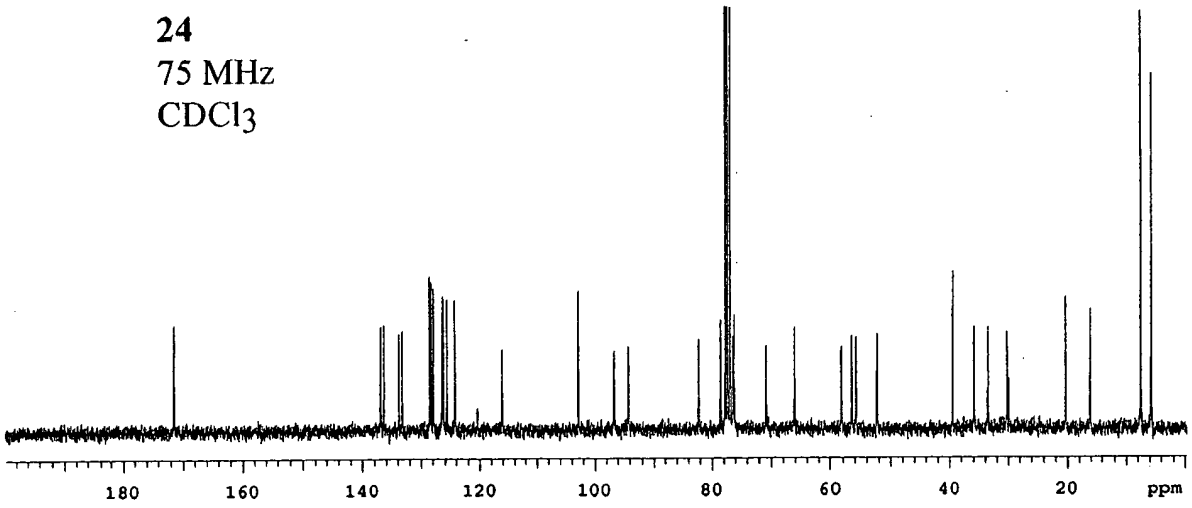


FIG. 34

24 1D-NOE Irradiation at 5.87 ppm
400 MHz
$CDCl_3$

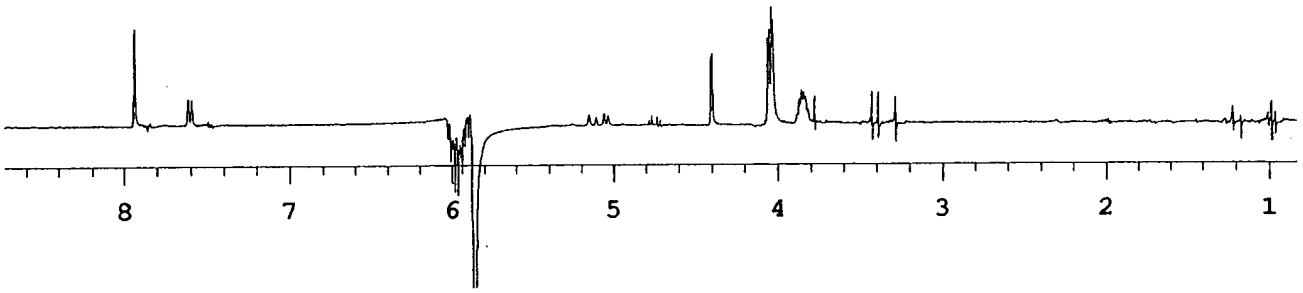


FIG. 35

24 1D-NOE Irradiation at 1.22 ppm
400 MHz
$CDCl_3$

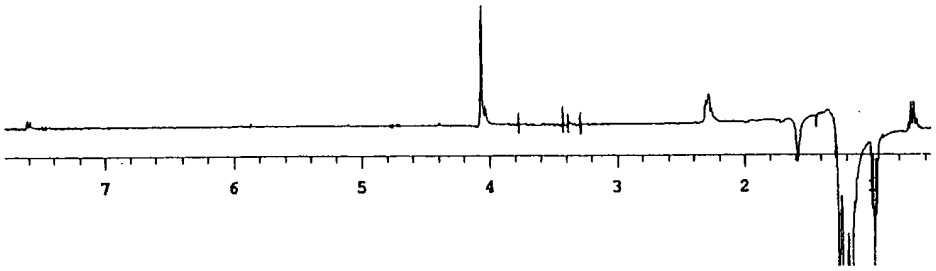


FIG. 36

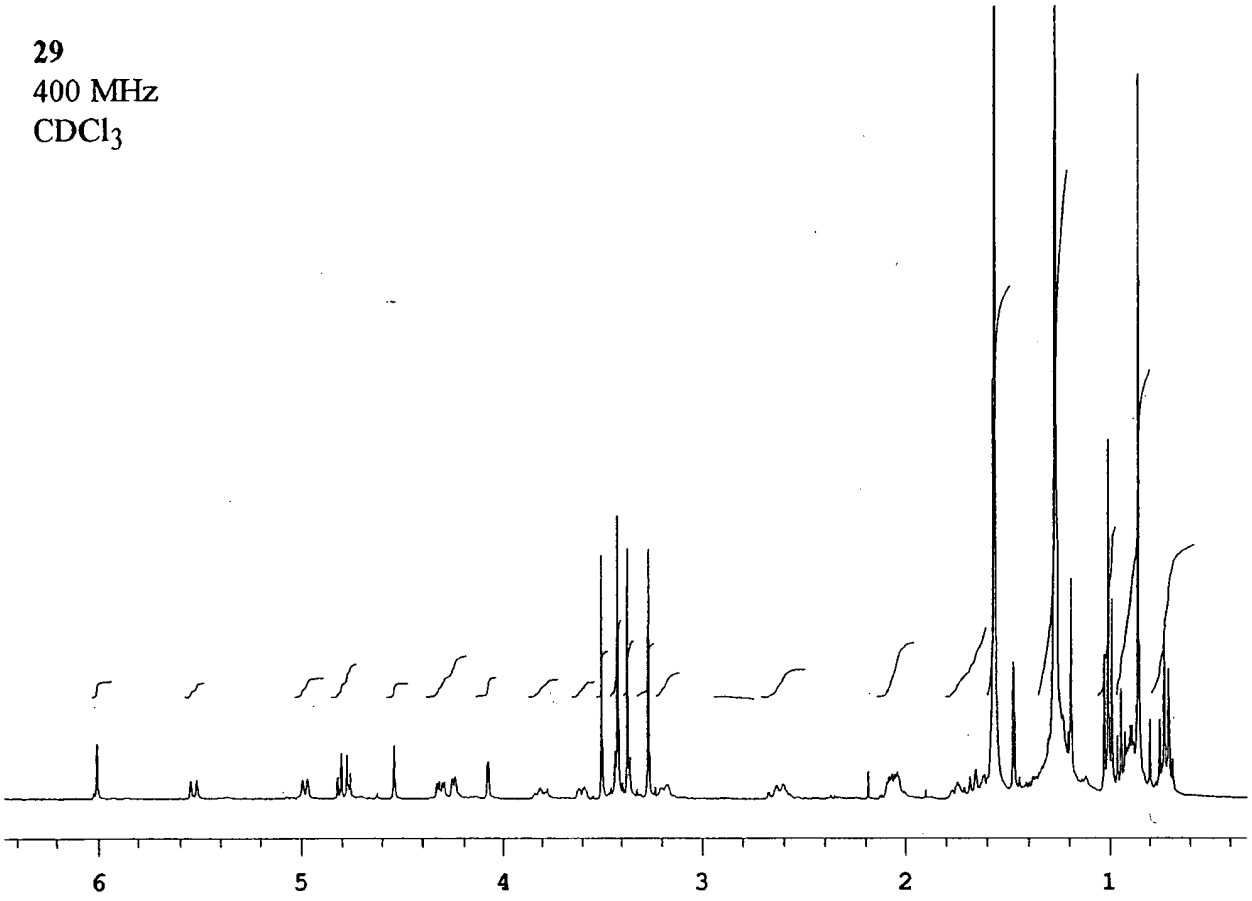


FIG. 37

29 1D-NOE Irradiation at 5.53 ppm
400 MHz
$CDCl_3$

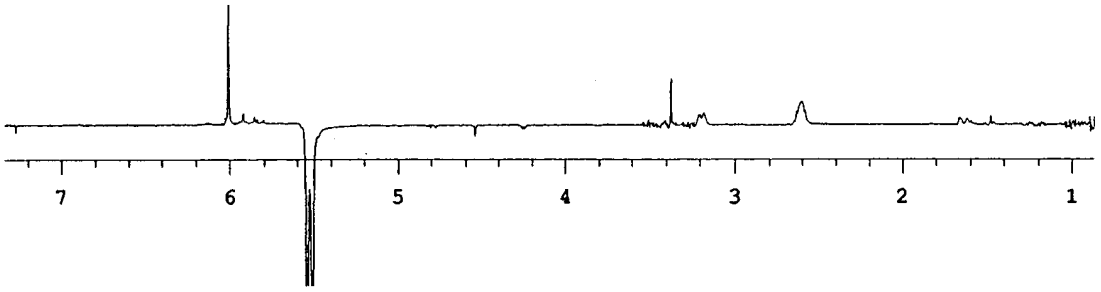


FIG. 38

29 1D-NOE Irradiation at 4.54 ppm
400 MHz
$CDCl_3$

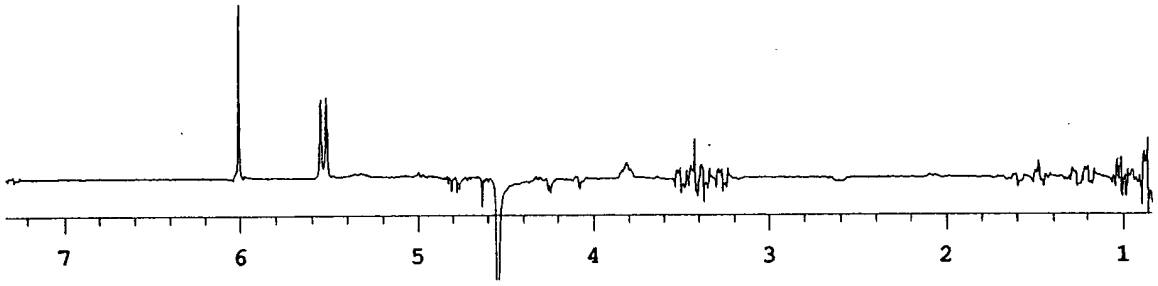


FIG. 39

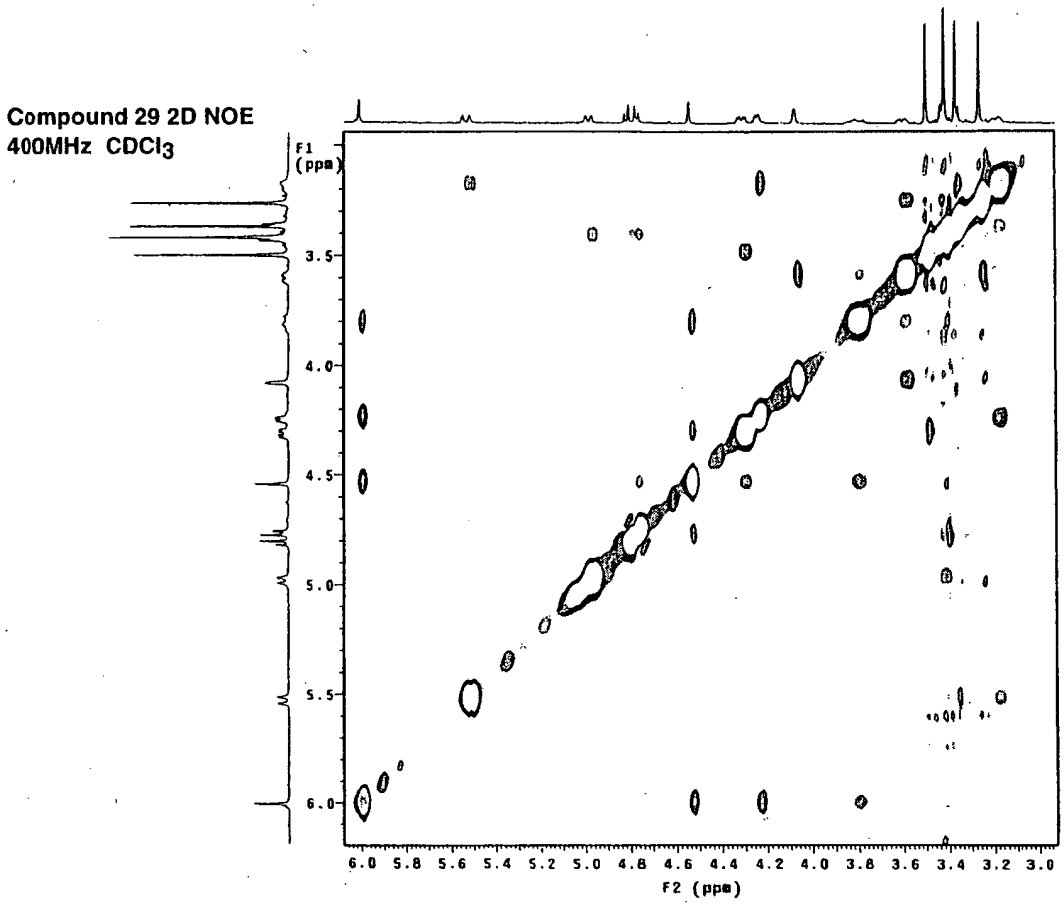

Compound 29 2D NOE
400MHz CDCl3
F1 (ppm)
3.5
4.0
4.5
5.0
5.5
6.0
6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0
F2 (ppm)

FIG. 40

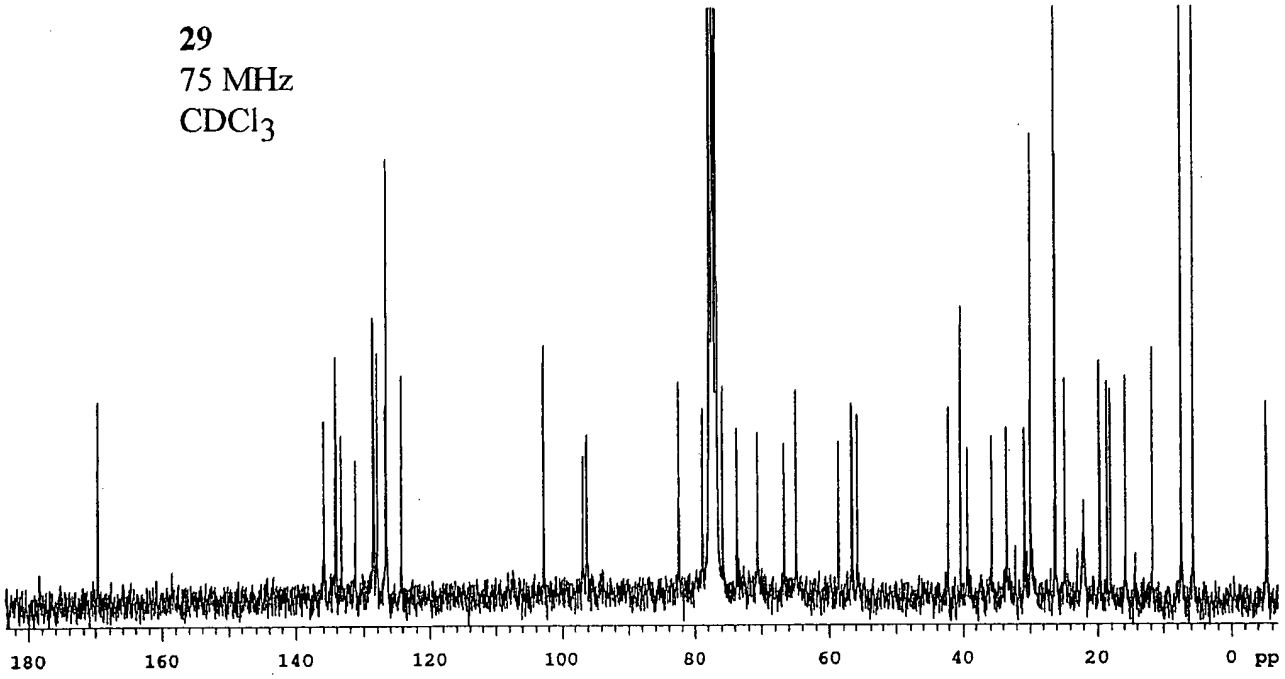


FIG. 41

30
400 MHz
$CDCl_3$

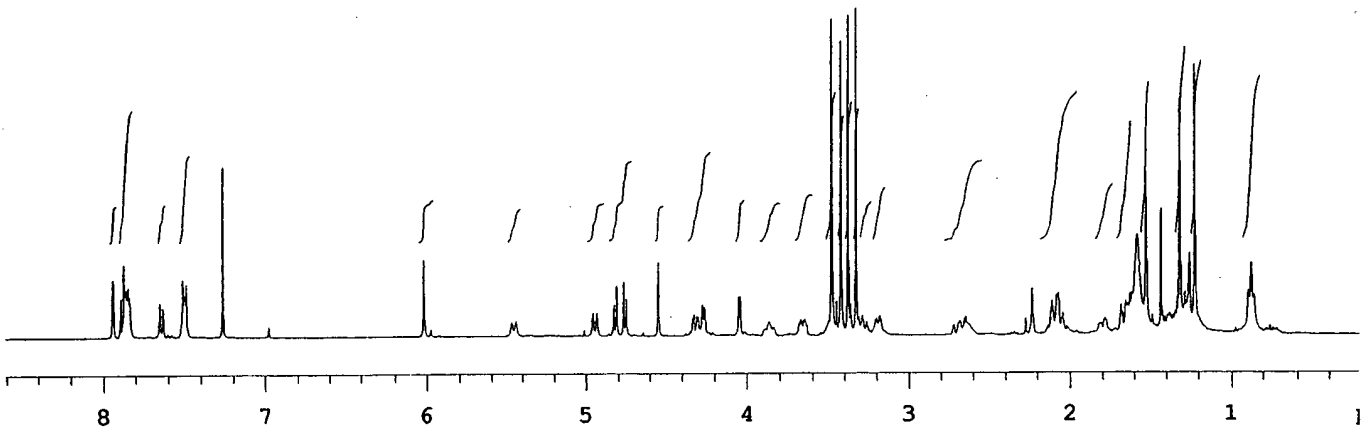


FIG. 42

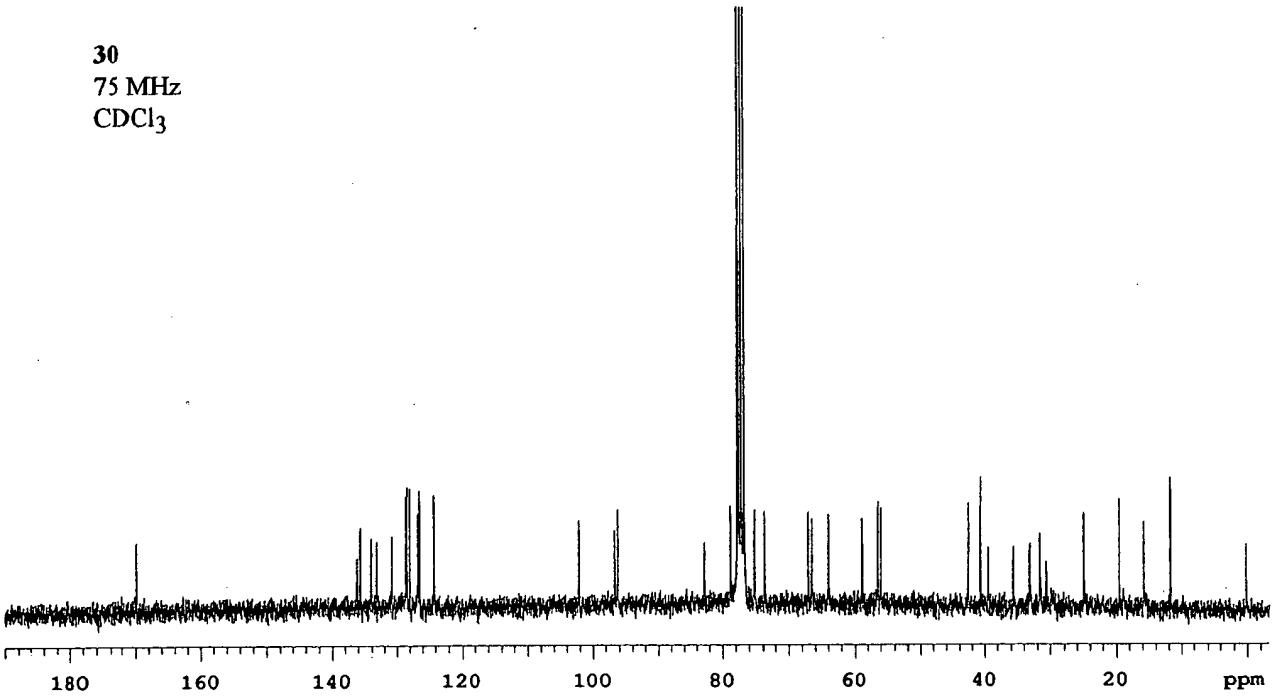


FIG. 43

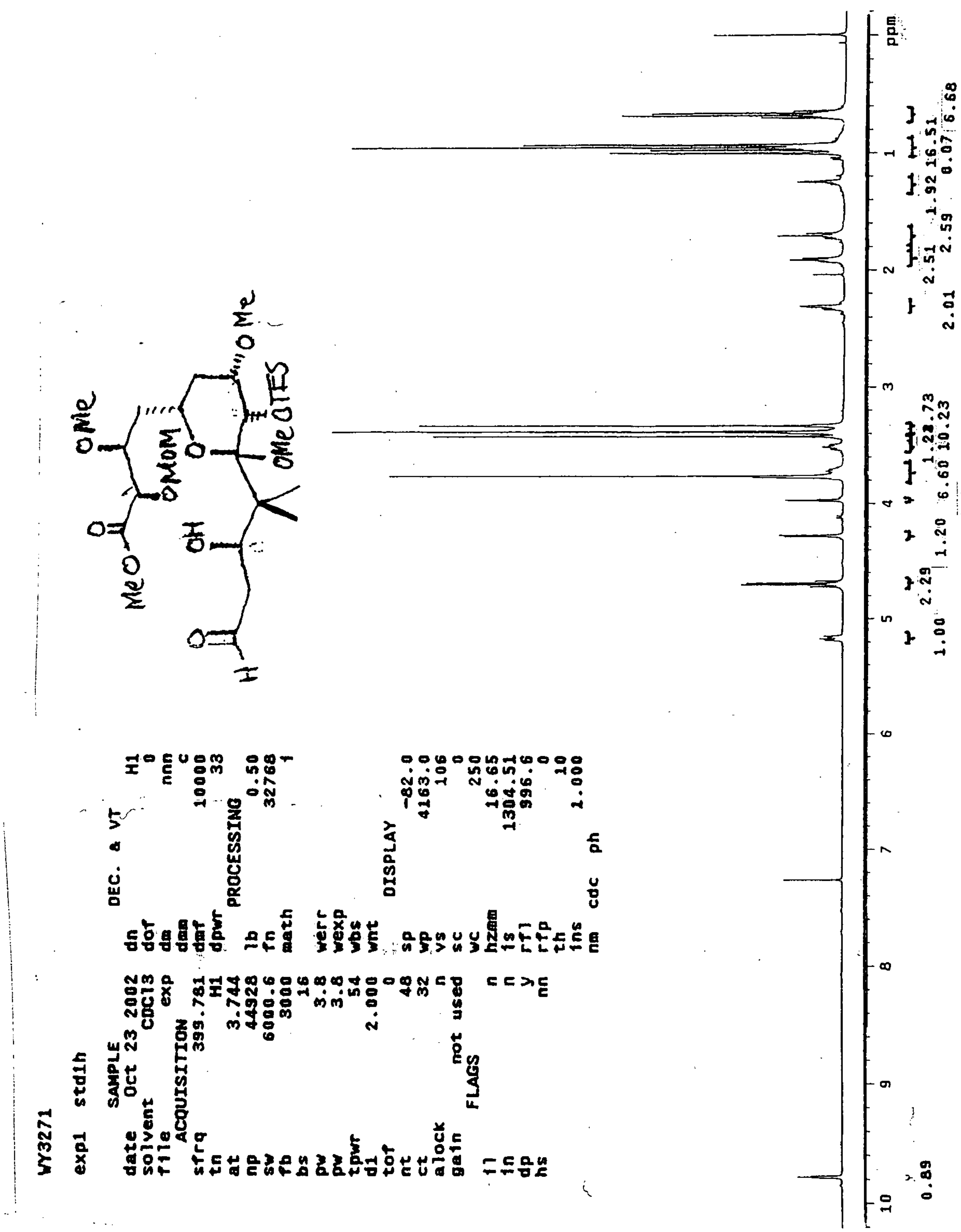

WY3271
expl stdlh
SAMPLE
date Oct 23 2002
solvent CDCl3
file exp
ACQUISITION
sfrq 399.781
tn H1
at 3.744
np 44928
sw 6000.6
fb 3000
bs 16
tpwr 54
d1 2.000
tof 0
nt 48
ct 32
alock n
gain not used
FLAGS
DEC. & VT
dn H1
dof 0
dm nnn
dmm c
dmf 10000
dpwr 33
PROCESSING
lb 0.50
fn 32768
DISPLAY
sp -82.0
wp 4163.0
vs 106
sc 0
wc 250
hzmm 16.65
th 10
ins 1.000
nm cdc ph
MeO
OMe
OMOM
OH
OTES
ppm

FIG. 44

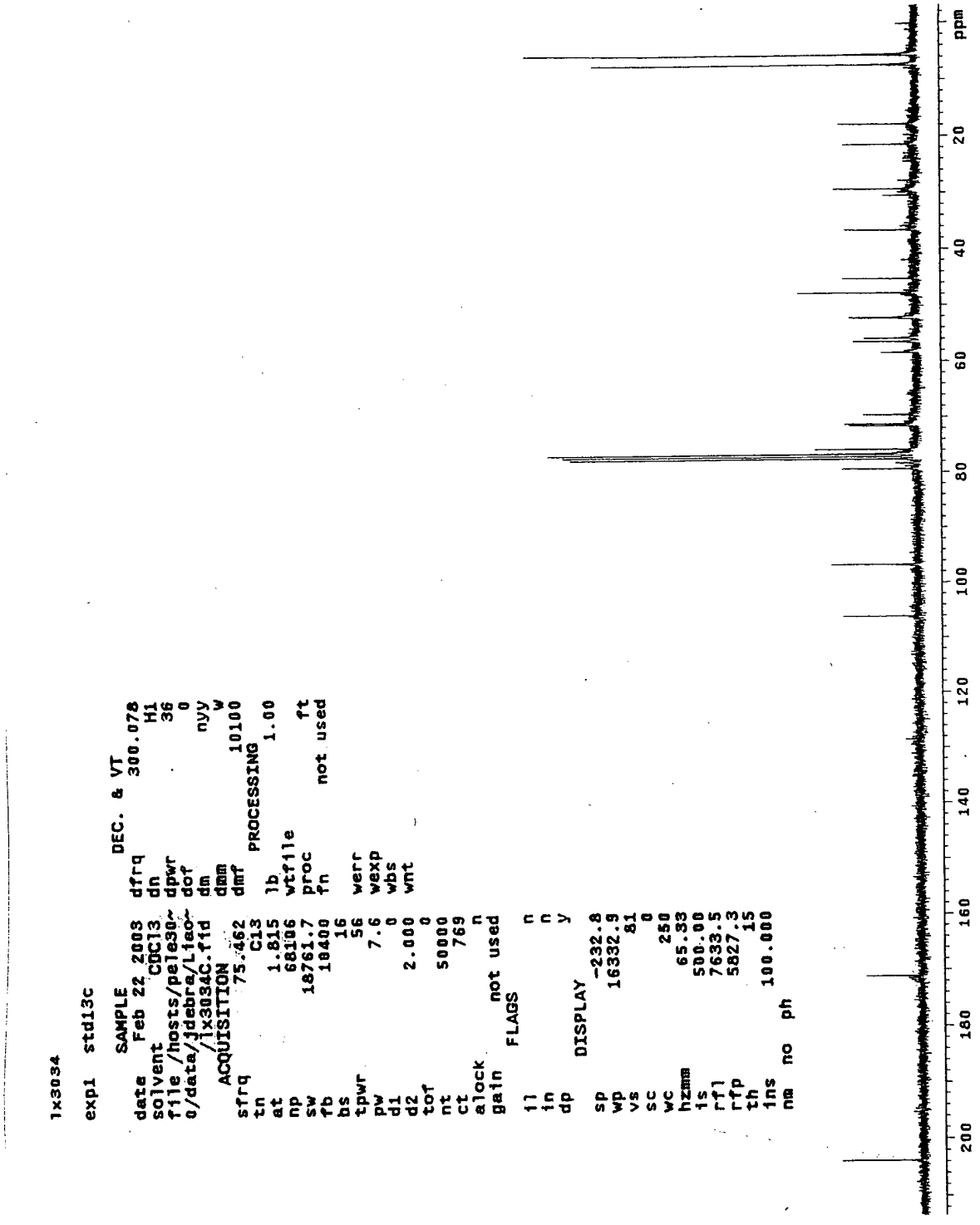

1x3034
expl std13c
SAMPLE
date Feb 22 2003
solvent CDCl3
file /hosts/pele30~
0/data/jdebra/Liao~
/1x3034C.fid
ACQUISITION
sfrq 75.462
tn C13
at 1.815
np 68106
sw 18761.7
fb 10400
bs 16
tpwr 56
pw 7.6
d1 0
d2 2.000
tof 0
nt 50000
ct 769
alock n
gain not used
FLAGS
il n
in n
dp y
DISPLAY
sp -232.8
wp 16332.9
vs 81
sc 0
wc 250
hzmm 65.33
is 500.00
rfl 7633.5
rfp 5827.3
th 15
ins 100.000
nm no ph
DEC. & VT
dfrq 300.078
dn H1
dpwr 36
dof 0
dm nyy
dmm w
dmf 10100
PROCESSING
lb 1.00
wtfile
proc ft
fn not used
werr
wexp
wbs
wnt
ppm
200
180
160
140
120
100
80
60
40
20

FIG. 45

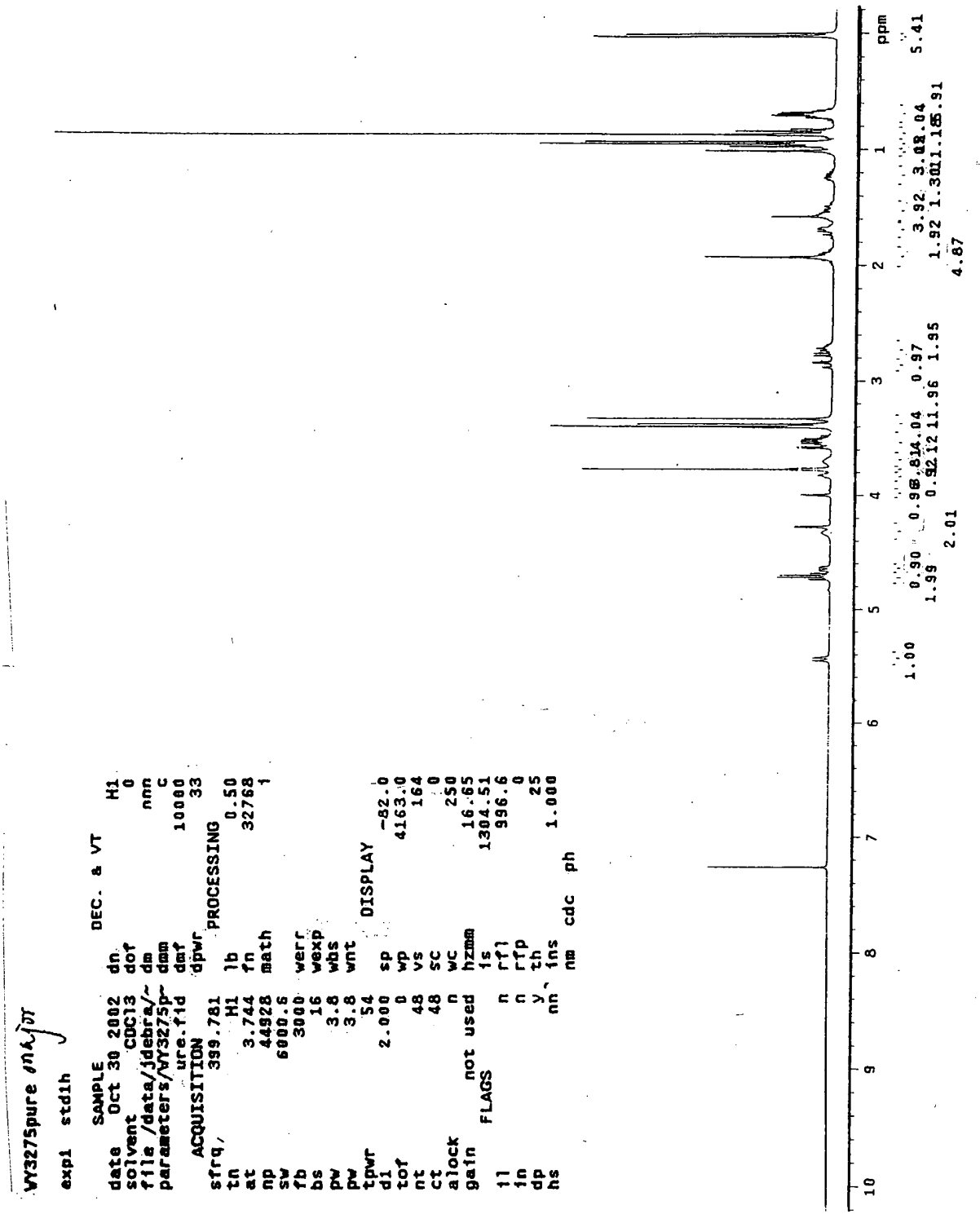

VY3275pure mAjor
expl stdih
SAMPLE
date Oct 30 2002
solvent CDCl3
file /data/jdebra/~
parameters/VY3275p~
ure.fid
ACQUISITION
sfrq 399.781
tn H1
at 3.744
np 44928
sw 6000.5
fb 3000
bs 16
pw 3.8
pw 3.8
tpwr 54
d1 2.000
tof 0
nt 48
ct 48
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DEC. & VT
dn H1
dof 0
dm nnn
dmm c
dmf 10000
dpwr 33
PROCESSING
lb 0.50
fn 32768
math 1
werr
wexp
wbs
wnt
DISPLAY
sp -82.0
wp 4163.0
vs 164
sc 0
wc 250
hzmm 16.65
is 1304.51
rfl 996.6
rfp 0
th 25
ins 1.000
nm cdc ph
1.00
0.90
1.99
2.01
0.98
0.92
4.04
12
11.96
0.97
1.95
3.92
1.92
3.04
1.30
1.18
4.87
5.41
5.91
ppm

FIG. 46

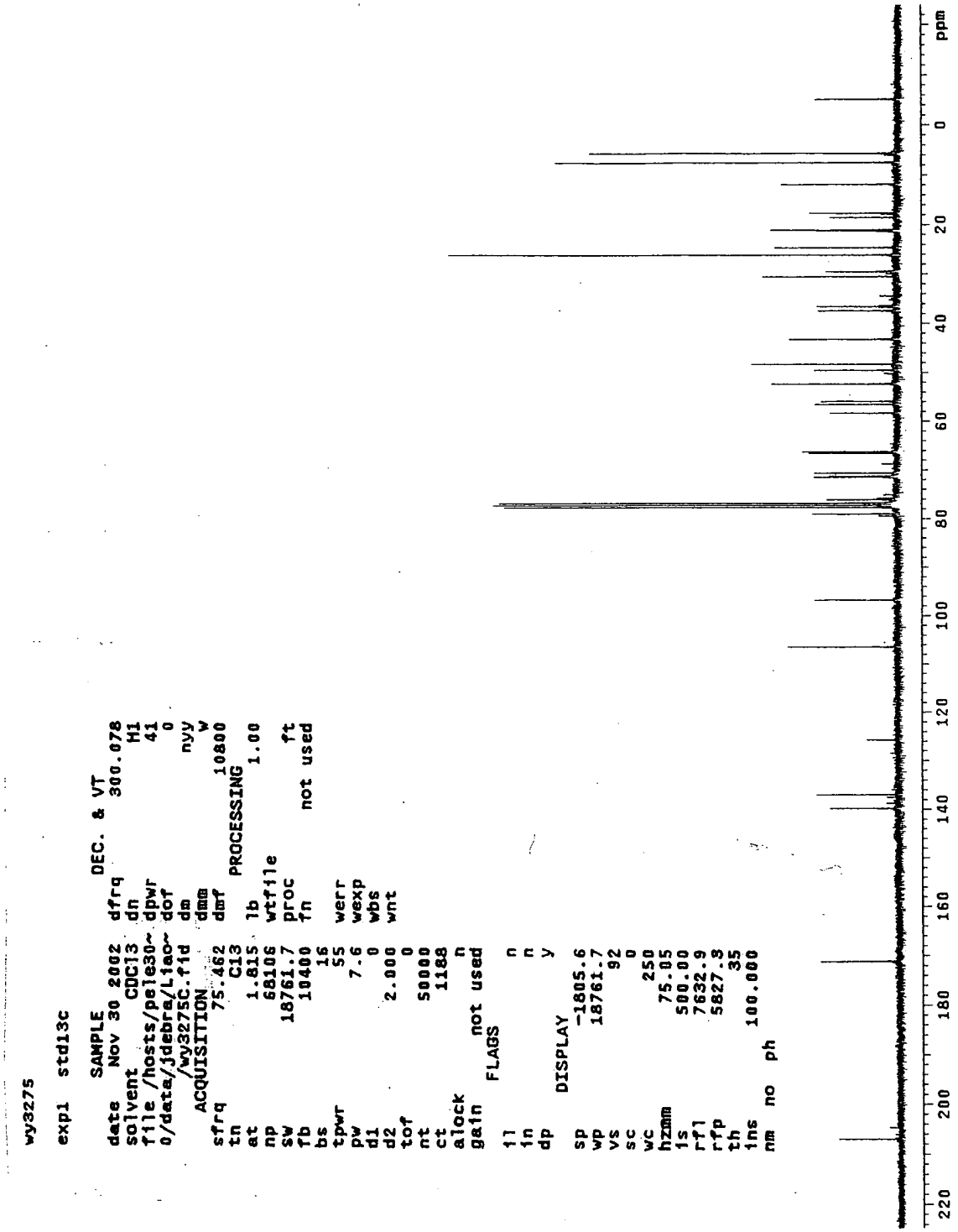

wy3275
expl std13c
SAMPLE
date Nov 30 2002
solvent CDCl3
file /hosts/pele30~
/data/jdebra/Liao~
/wy3275C.fid
ACQUISITION
sfrq 75.462
tn C13
at 1.815
np 68108
sw 18761.7
fb 10400
bs 16
tpwr 55
pw 7.6
d1 0
d2 2.000
tof 0
nt 50000
ct 1188
alock n
gain not used
FLAGS
DEC. & VT
dfrq 300.078
dn H1
dpwr 41
dof 0
dm nyy
dmm w
dmf 10800
PROCESSING
lb 1.00
wtfile
proc ft
fn not used
werr
wexp
wbs
wnt
il n
in n
dp y
DISPLAY
sp -1805.6
wp 18761.7
vs 92
sc 0
wc 250
hzmm 75.05
is 500.00
rfl 7632.9
rfp 5827.3
th 35
ins 100.000
nm no ph
220
200
180
160
140
120
100
80
60
40
20
0
ppm

FIG. 47

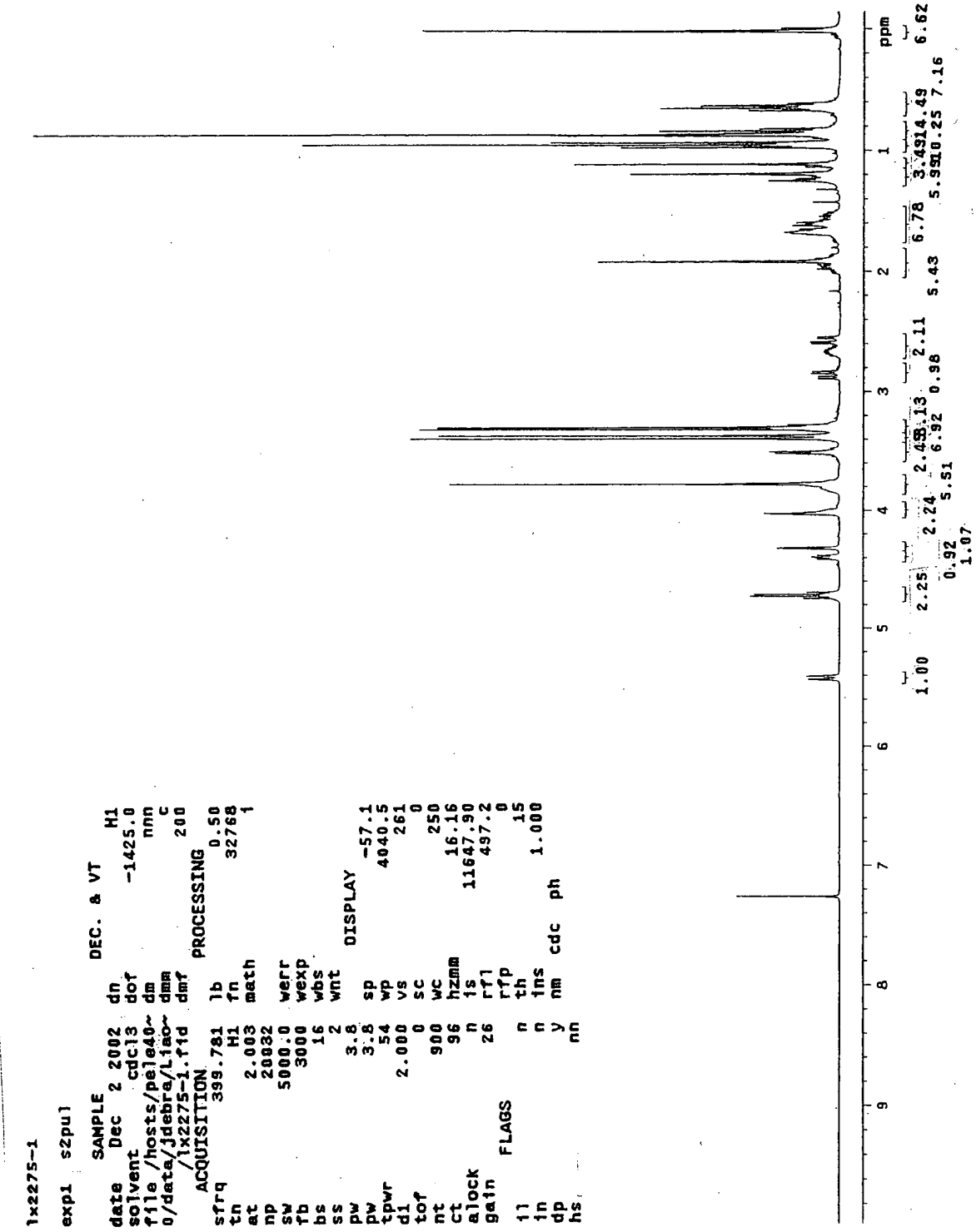

1x2275-1
exp1 s2pul
SAMPLE
date Dec 2 2002
solvent cdcl3
file /hosts/pele40~
0/data/jdebra/Liao~
/1x2275-1.fid
ACQUISITION
sfrq 399.781
tn H1
at 2.003
np 20032
sw 5000.0
fb 3000
bs 16
ss 2
pw 3.8
pw 3.8
tpwr 54
d1 2.000
tof 0
nt 900
ct 96
alock n
gain 26
FLAGS
il n
in n
dp y
hs nn
DEC. & VT
dn H1
dof -1425.0
dm nnn
dmm c
dmf 200
PROCESSING
lb 0.50
fn 32768
math 1
werr
wexp
wbs
wnt
DISPLAY
sp -57.1
wp 4040.5
vs 261
sc 0
wc 250
hzmm 16.16
is 11647.90
rf1 497.2
rfp 0
th 15
ins 1.000
cdc ph
nm
1.00
2.25
0.92
1.07
2.24
5.51
2.45
6.92
3.13
0.98
2.11
5.43
6.78
5.93
3.49
10.25
14.49
7.16
6.62
ppm

FIG. 48

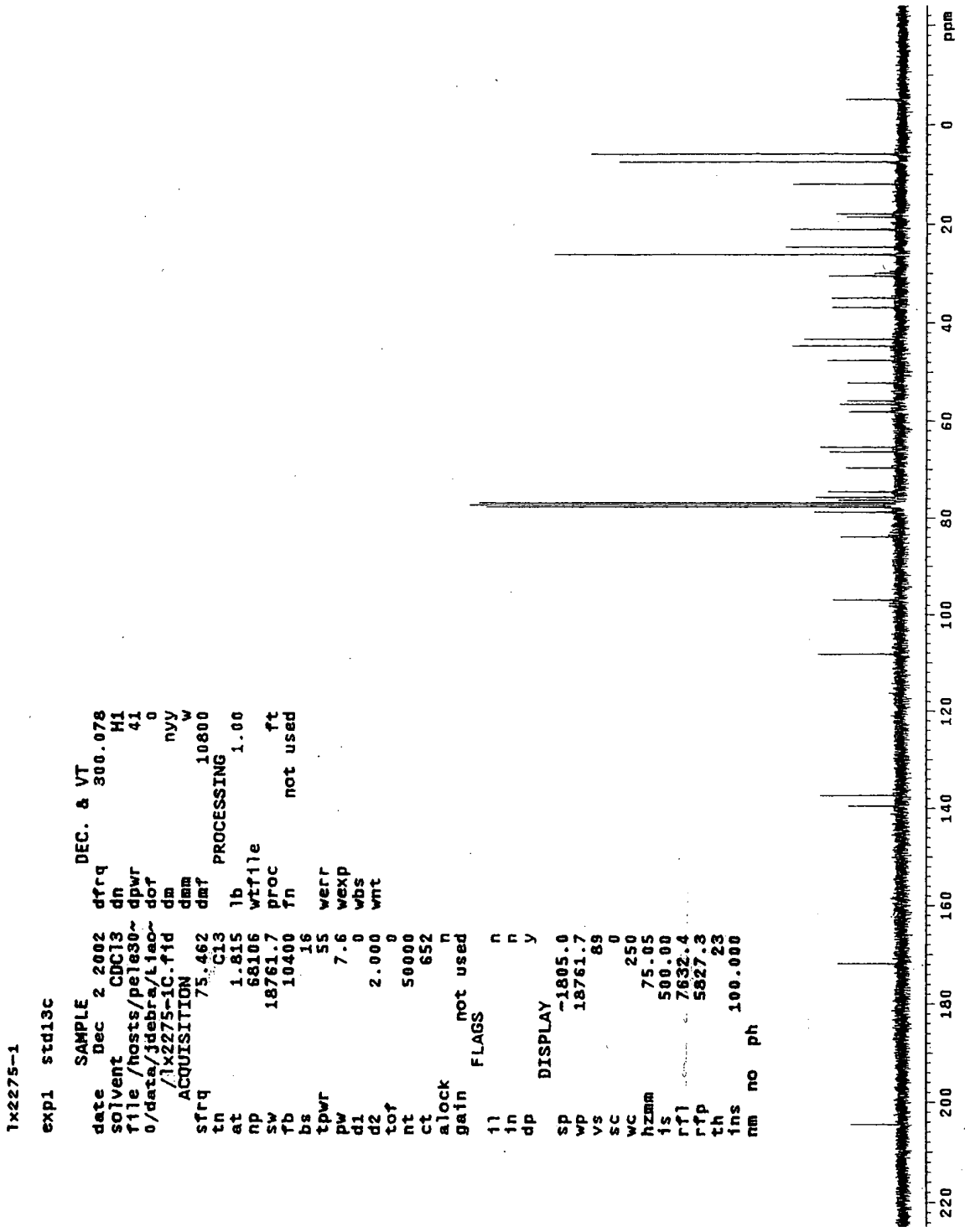

1x2275-1
expl std13c
SAMPLE
date Dec 2 2002
solvent CDCl3
file /hosts/pele30~
o/data/jdebra/Liao~
/1x2275-1C.fid
ACQUISITION
sfrq 75.462
tn C13
at 1.815
np 68106
sw 18761.7
fb 10400
bs 16
tpwr 55
pw 7.6
d1 0
d2 2.000
tof 0
nt 50000
ct 652
alock n
gain not used
DEC. & VT
dfrq 300.078
dn H1
dpwr 41
dof 0
dm nyy
dmm w
dmf 10800
PROCESSING
lb 1.00
wtfile
proc ft
fn not used
werr
wexp
wbs
wnt
n
n
y
FLAGS
DISPLAY
sp -1805.0
wp 18761.7
vs 89
sc 0
wc 250
hzmm 75.05
is 500.00
rfl 7632.4
rfp 5827.3
th 23
ins 100.000
nm no ph
ppm

FIG. 49

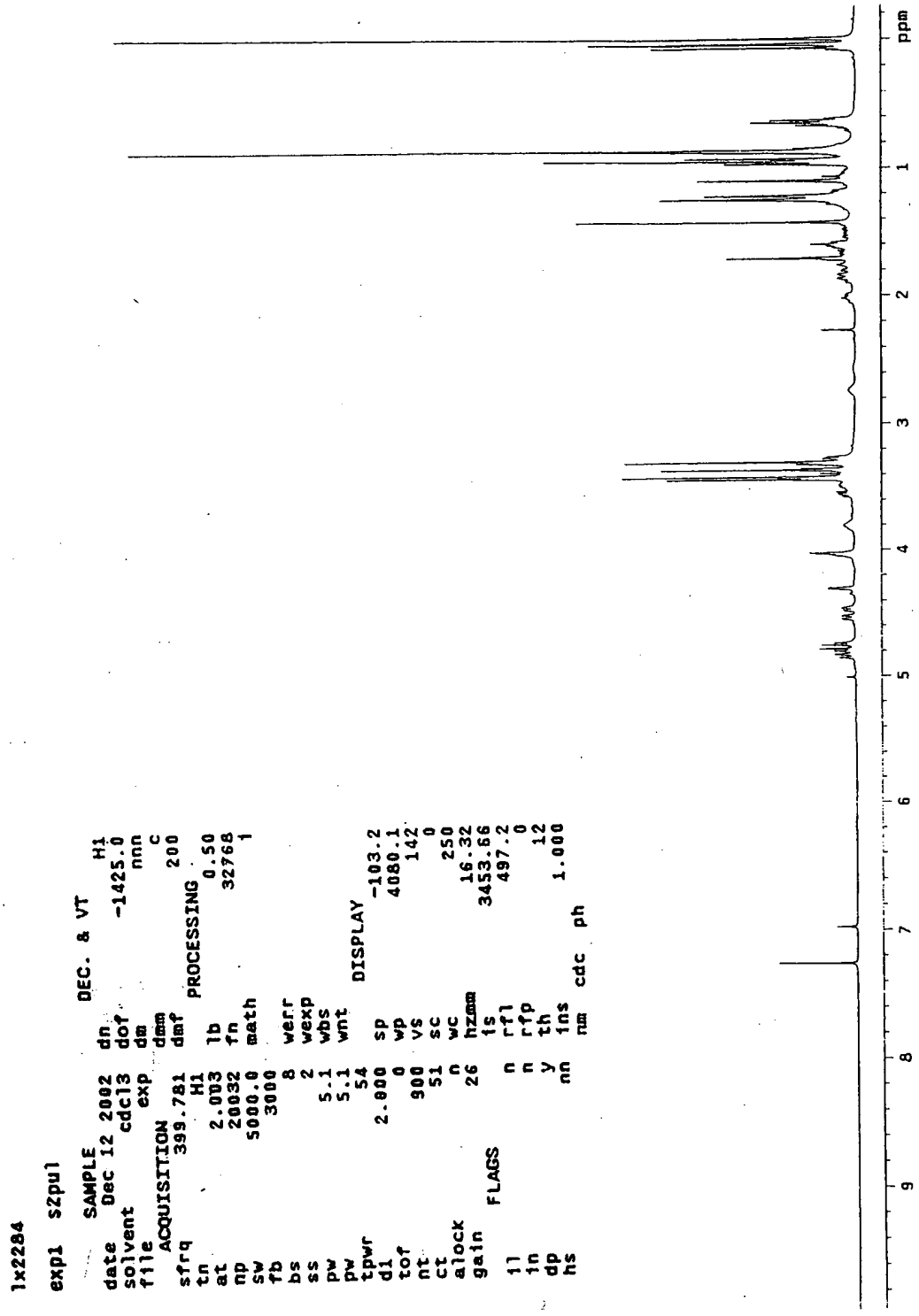

1x2284
expl s2pul
SAMPLE
date Dec 12 2002
solvent cdcl3
file exp
ACQUISITION
sfrq 399.781
tn H1
at 2.003
np 20032
sw 5000.0
fb 3000
bs 8
ss 2
pw 5.1
pw 5.1
tpwr 54
d1 2.000
tof 0
nt 900
ct 51
alock n
gain 26
FLAGS
il n
in n
dp y
hs nn
DEC. & VT
dn H1
dof -1425.0
dm nnn
dmm c
dmf 200
PROCESSING
lb 0.50
fn 32768
math 1
werr
wexp
wbs
wnt
DISPLAY
sp -103.2
wp 4080.1
vs 142
sc 0
wc 250
hzmm 16.32
is 3453.66
rfl 497.2
rfp 0
th 12
ins 1.000
nm cdc ph
ppm
9
8
7
6
5
4
3
2
1

FIG. 50

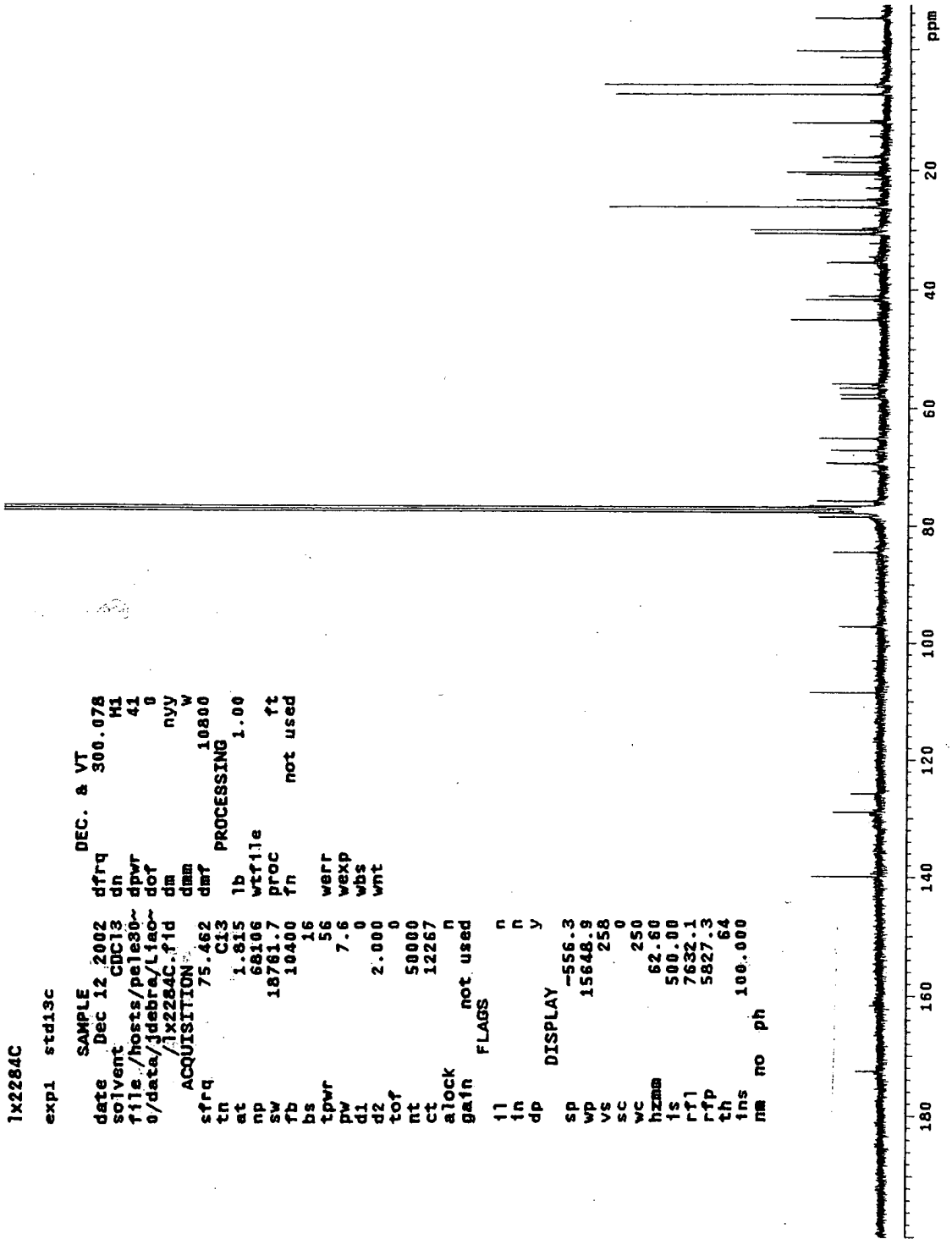

1x2284C
exp1 std13c
SAMPLE
date Dec 12 2002
solvent CDCl3
file /hosts/pele30~/pele30/data/debra/Liao~/1x2284C.fid
ACQUISITION
sfrq 75.462
tn C13
at 1.815
np 68106
sw 18761.7
fb 10400
bs 16
tpwr 56
pw 7.6
d1 0
d2 2.000
tof 0
nt 50000
ct 12267
alock n
gain not used
FLAGS
il n
in n
dp y
DISPLAY
sp -556.3
wp 15648.9
vs 258
sc 0
wc 250
hzmm 62.60
is 500.00
rfl 7632.1
rfp 5827.3
th 64
ins 100.000
DEC. & VT
dfrq 300.078
dn H1
dpwr 41
dof 0
dm nyy
dmm w
dmf 10800
PROCESSING
lb 1.00
wtfile ft
proc ft
fn not used
werr
wexp
wbs
wnt
nm no ph
ppm
180
160
140
120
100
80
60
40
20

FIG. 51

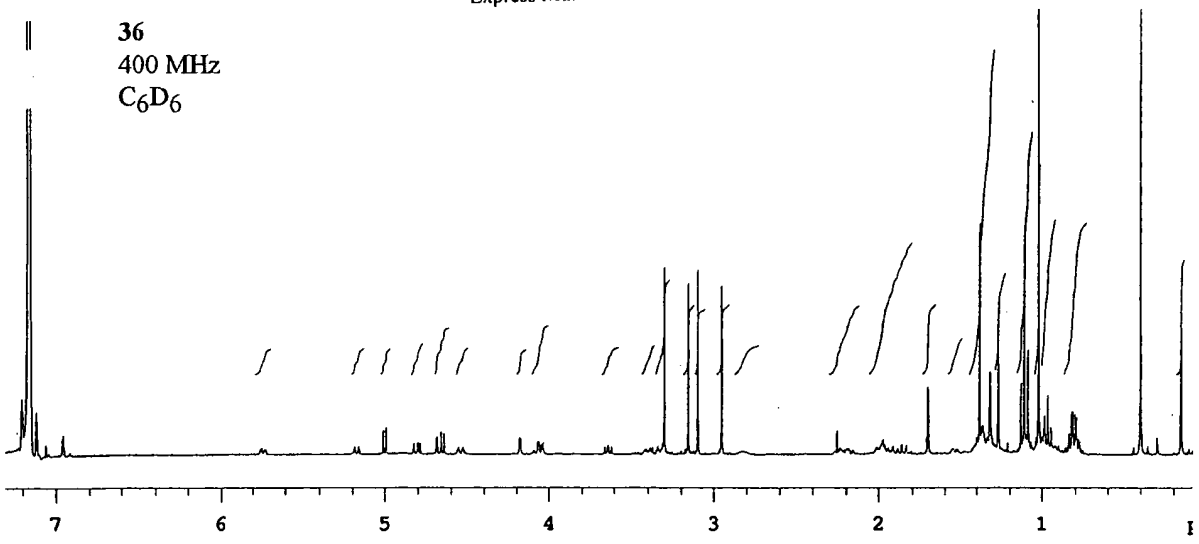


FIG. 52

36 1D-NOE Irradiation at 5.74 ppm
400 MHz
C_6D_6

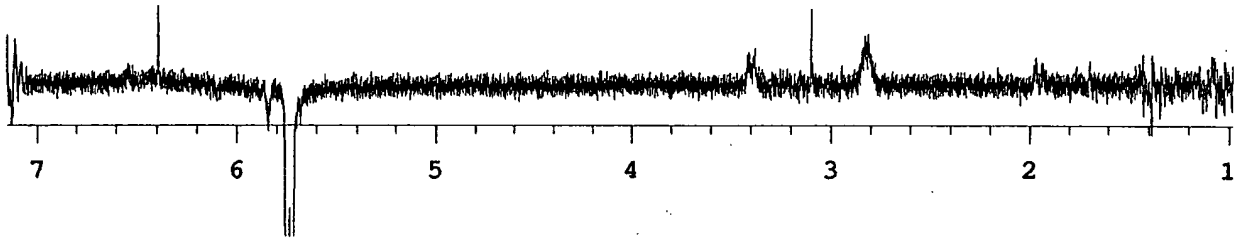


FIG. 53

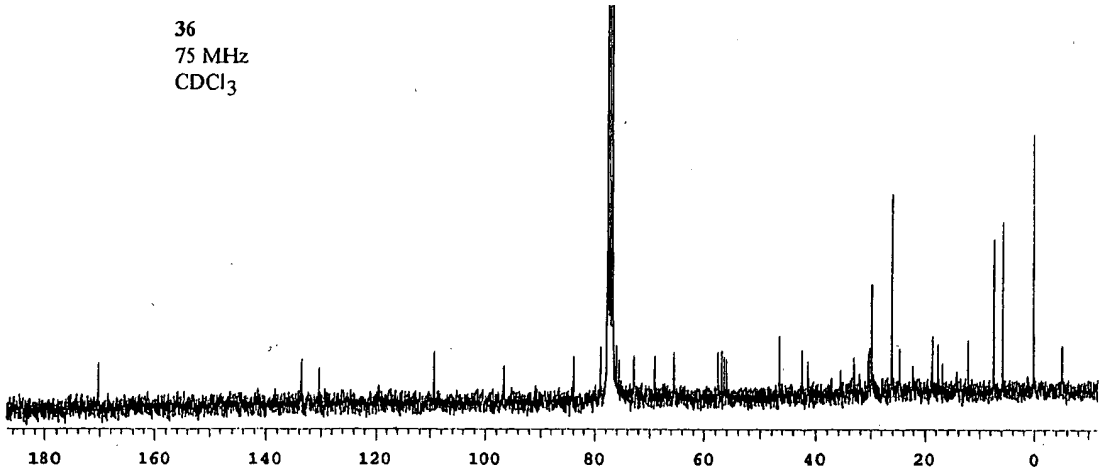


FIG. 54

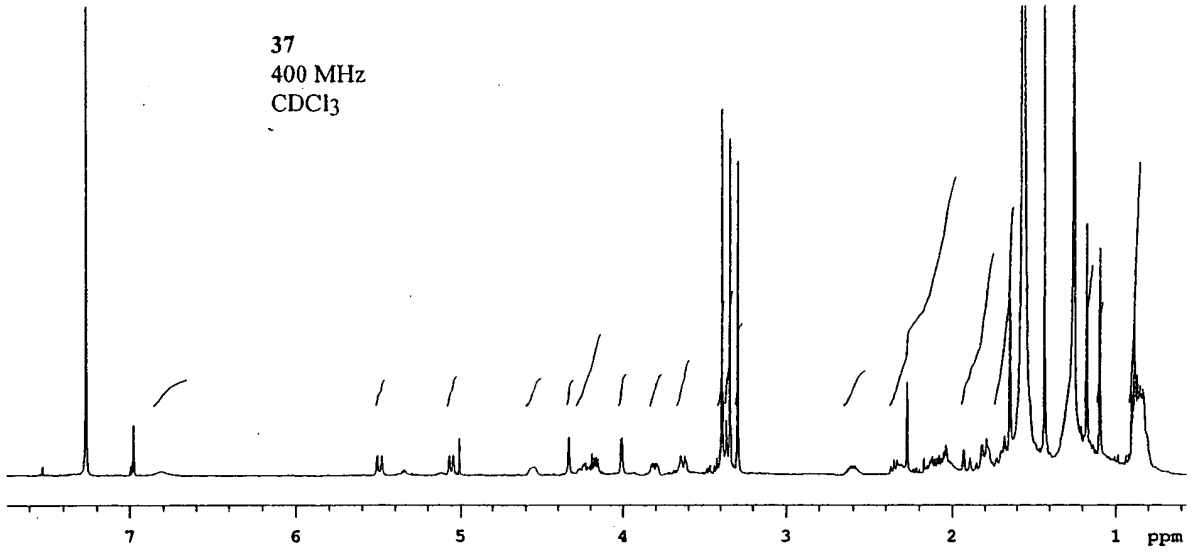


FIG. 55

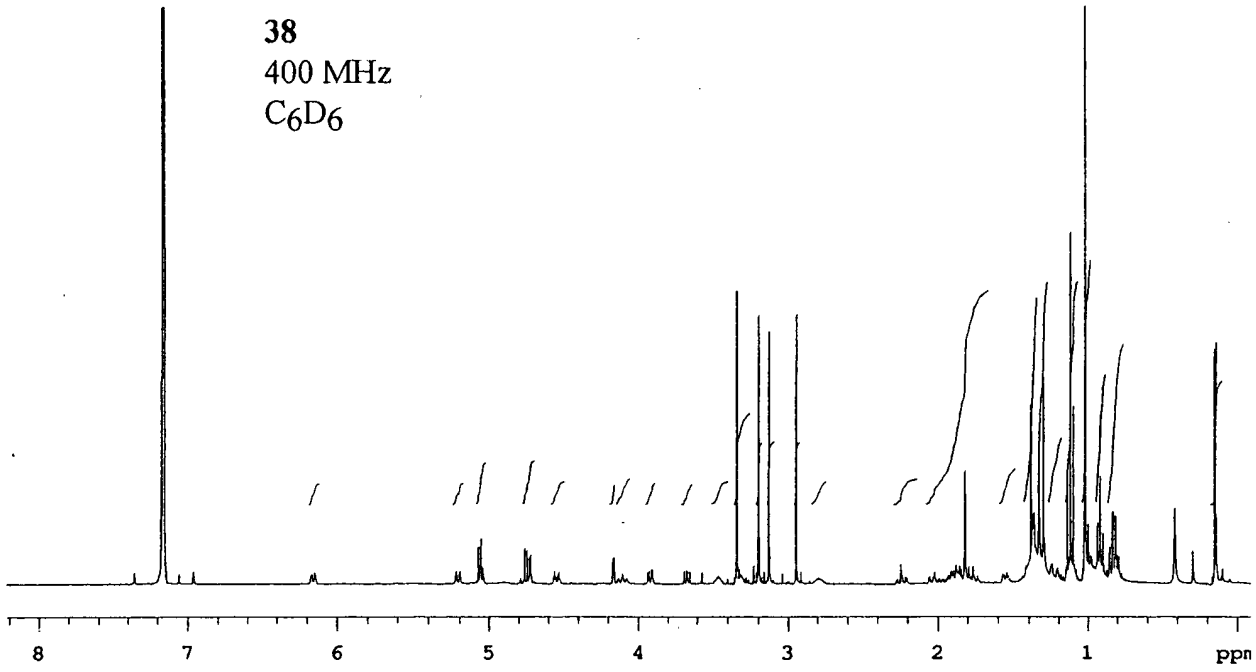


FIG. 56

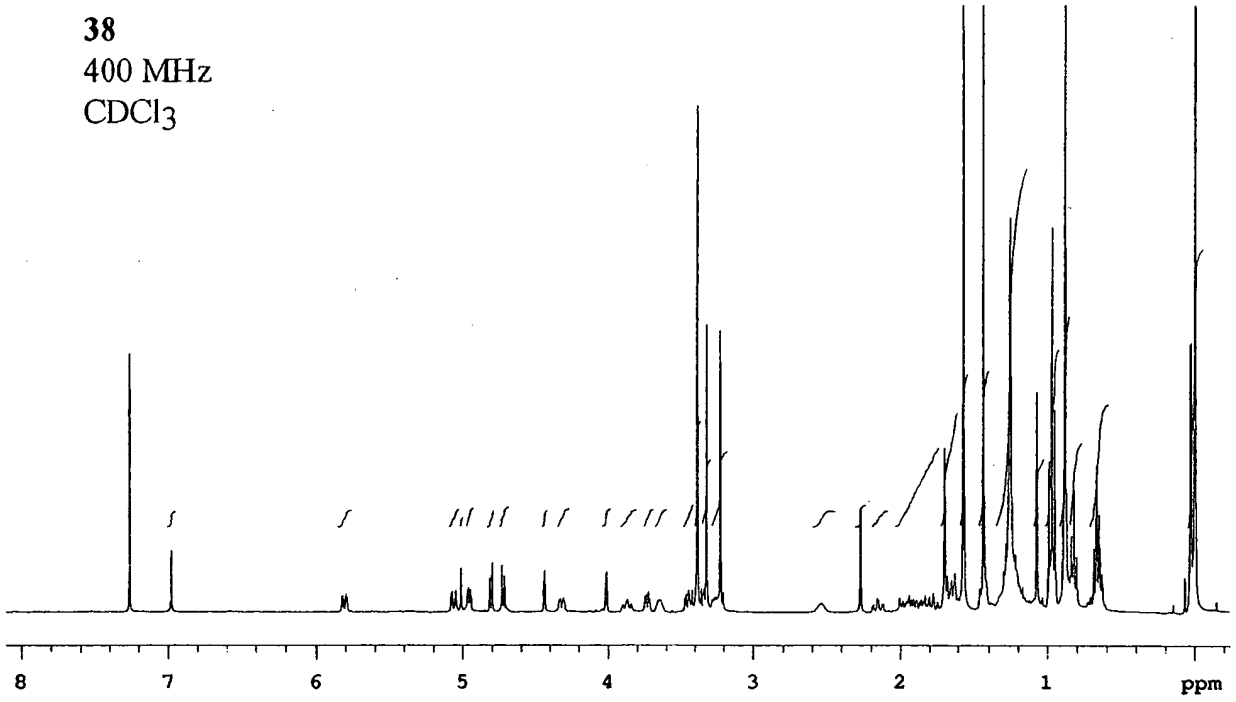


FIG. 57

38 1D-NOE Irradiation at 6.16 ppm
400 MHz
C_6D_6

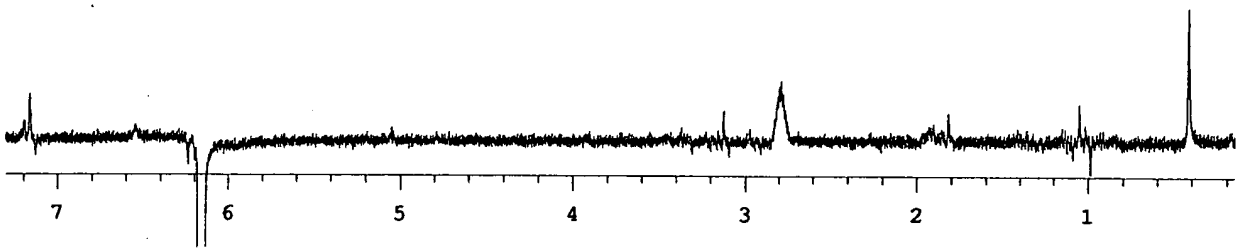


FIG. 58

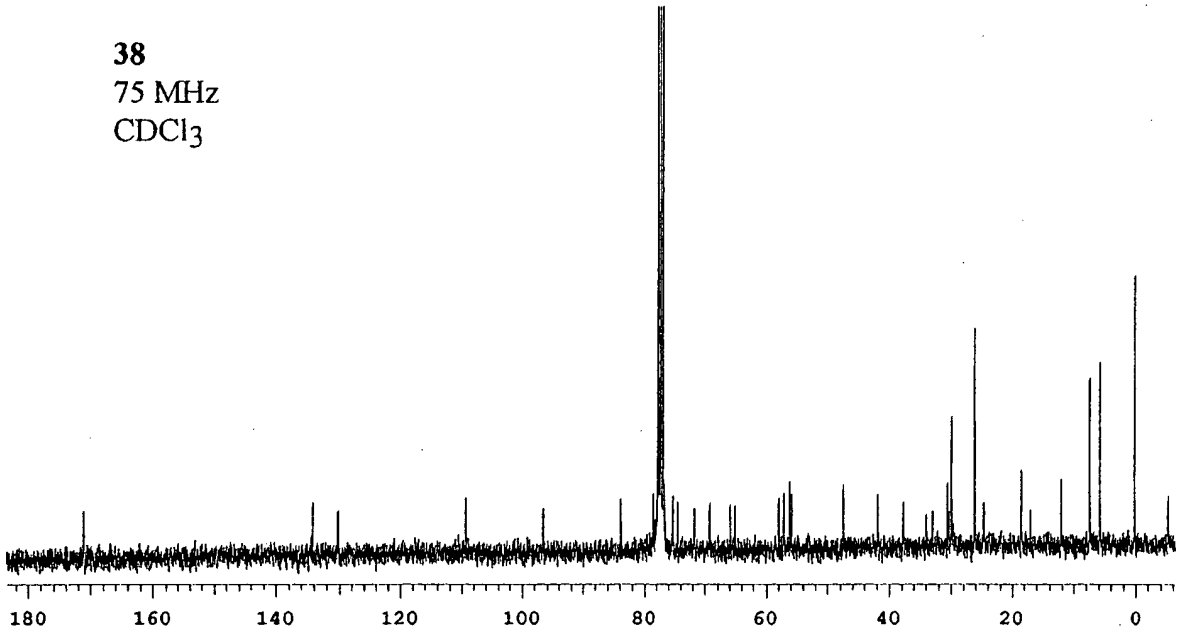


FIG. 59

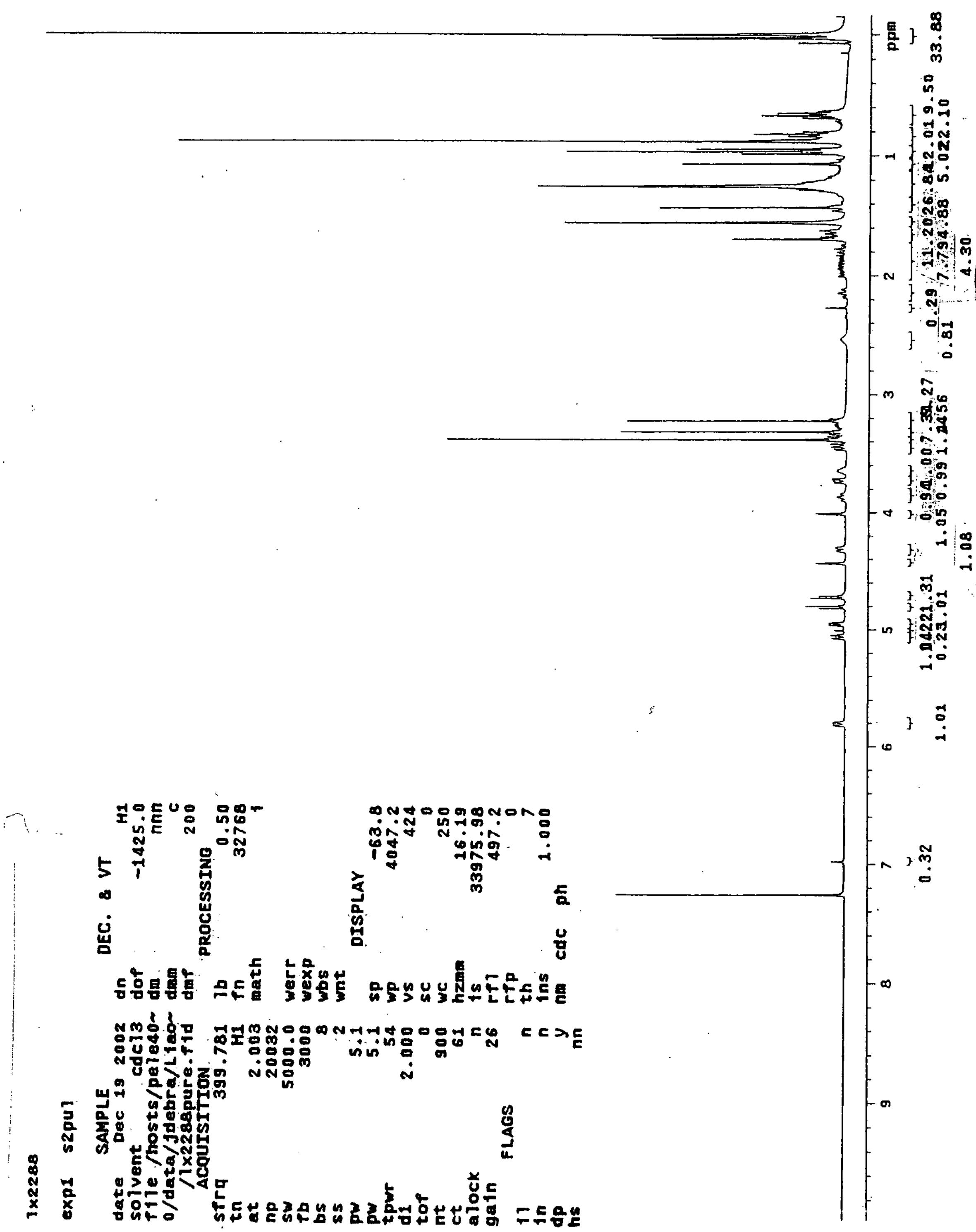

1x2288
exp1 s2pul
SAMPLE
date Dec 19 2002
solvent cdcl3
file /hosts/pele40~
0/data/jdebra/Liao~
/lx2288pure.fid
ACQUISITION
sfrq 399.781
tn H1
at 2.003
np 20032
sw 5000.0
fb 3000
bs 8
ss 2
pw 5.1
pw 5.1
tpwr 54
d1 2.000
tof 0
nt 900
ct 61
alock n
gain 26
FLAGS
il n
in n
dp y
hs nn
DEC. & VT
dn H1
dof -1425.0
dm nnn
dmm c
dmf 200
PROCESSING
lb 0.50
fn 32768
math f
werr
wexp
wbs
wnt
DISPLAY
sp -63.8
wp 4047.2
vs 424
sc 0
wc 250
hzmm 16.19
is 33975.98
rfl 497.2
rfp 0
th 7
ins 1.000
nm cdc ph
ppm

FIG. 60

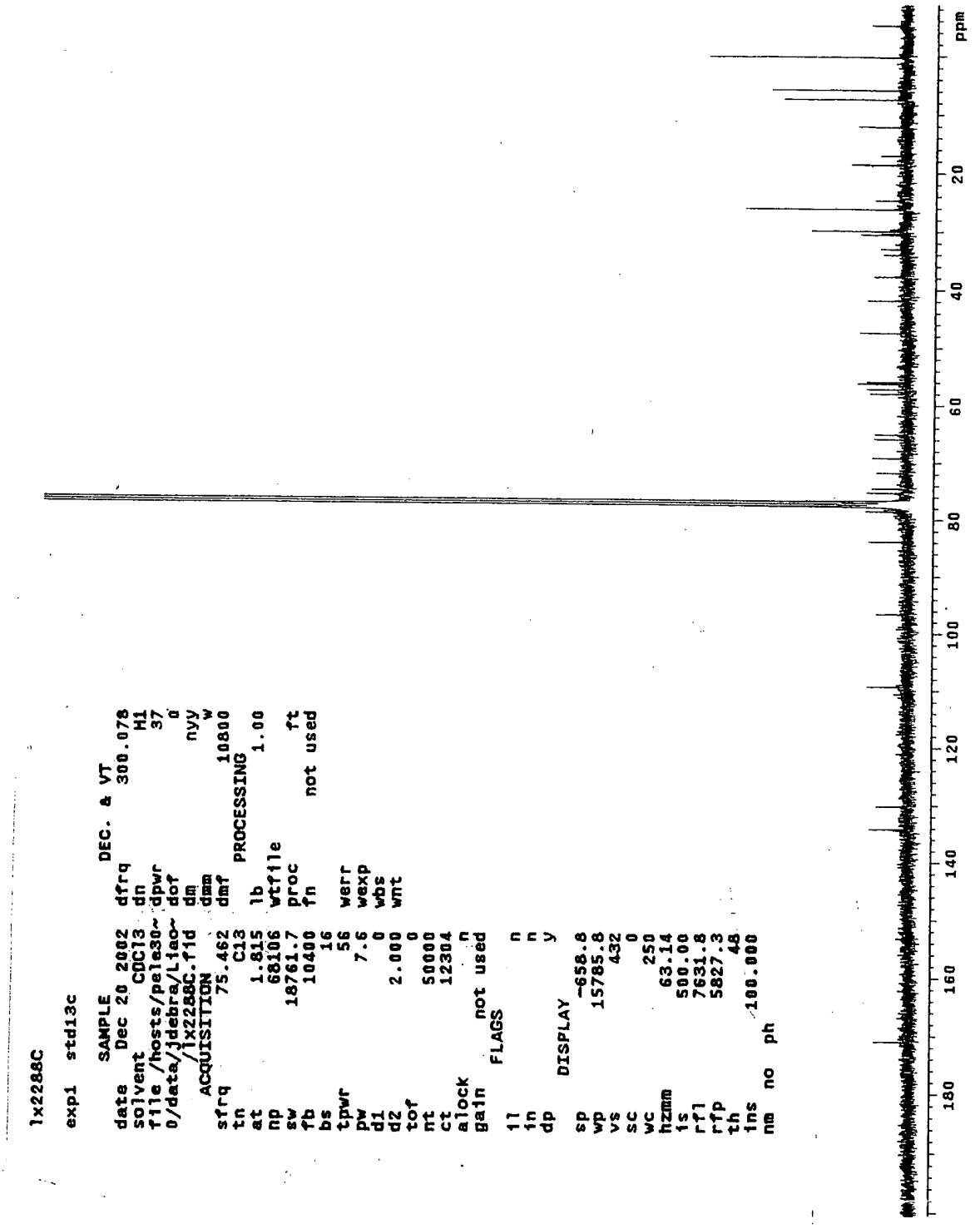

1x2288C
expl std13c
SAMPLE
date Dec 20 2002
solvent CDCl3
file /hosts/pela30~
0/data/jdebra/Liao~
/1x2288C.fid
ACQUISITION
sfrq 75.462
tn C13
at 1.815
np 68106
sw 18761.7
fb 10400
bs 16
tpwr 56
pw 7.6
d1 0
d2 2.000
tof 0
nt 50000
ct 12304
alock n
gain not used
DEC. & VT
dfrq 300.078
dn H1
dpwr 37
dof 0
dm nyy
dmm w
dmf 10800
PROCESSING
lb 1.00
wtfile
proc ft
fn not used
werr
wexp
wbs
wnt
FLAGS
il n
in n
dp y
DISPLAY
sp -658.8
wp 15785.8
vs 432
sc 0
wc 250
hzmm 63.14
is 500.00
rfl 7631.8
rfp 5827.3
th 48
ins 100.000
nm no ph
180
160
140
120
100
80
60
40
20
ppm

FIG. 61

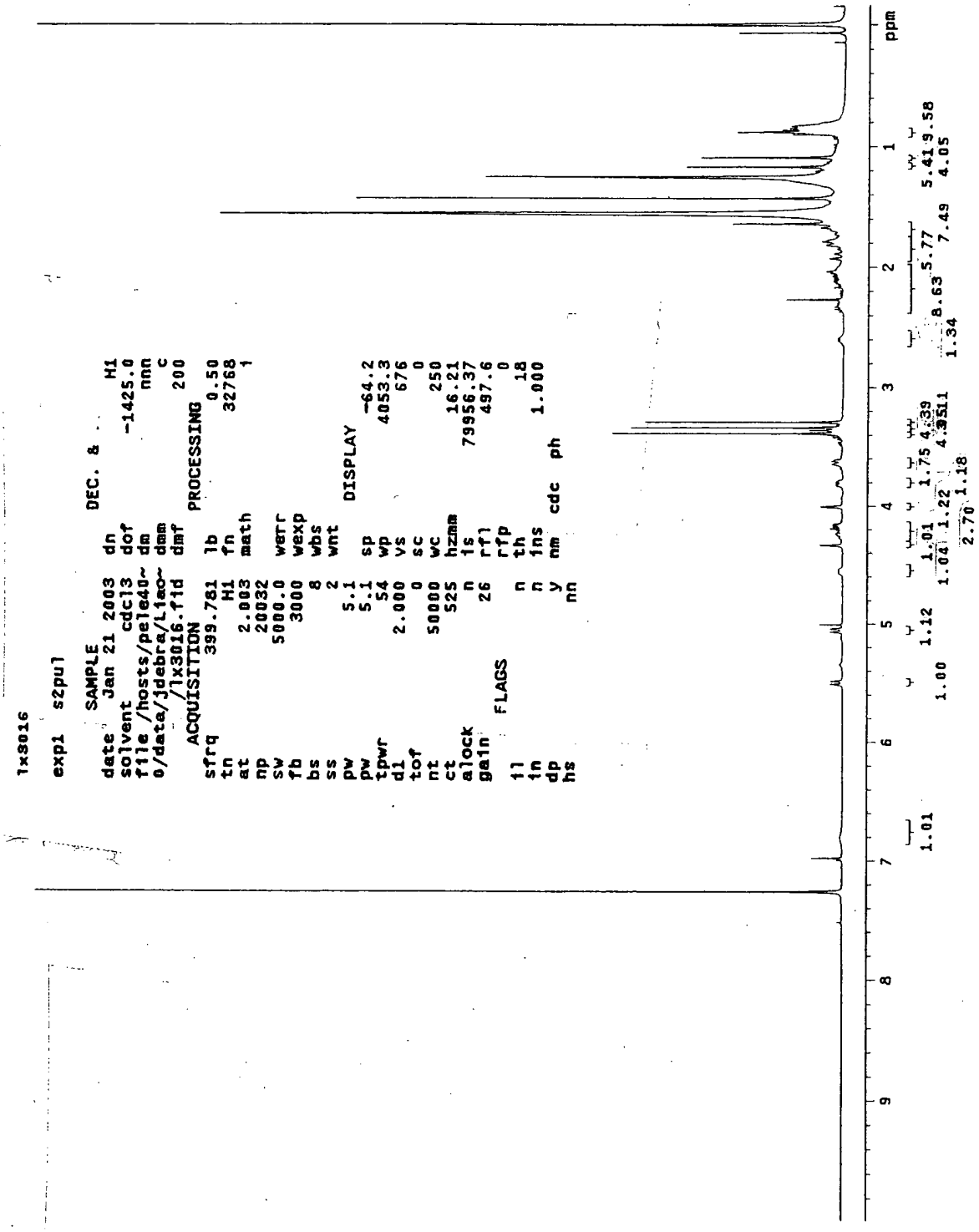

1x3016
expl s2pul
SAMPLE
date Jan 21 2003
solvent cdcl3
file /hosts/pele40~
o/data/jdebra/L1ac~
/1x3016.fid
ACQUISITION
sfrq 399.781
tn H1
at 2.003
np 20032
sw 5000.0
fb 3000
bs 8
ss 2
pw 5.1
pw 5.1
tpwr 54
d1 2.000
tof 0
nt 50000
ct 525
alock n
gain 26
FLAGS
DEC. & ..
dn H1
dof -1425.0
dm nnn
dmm c
dmf 200
PROCESSING
lb 0.50
fn 32768
math 1
werr
wexp
wbs
wnt
DISPLAY
sp -64.2
wp 4053.3
vs 676
sc 0
wc 250
hzmm 16.21
is 79956.37
rf1 497.6
rfp 0
rfl 0
th 18
ins 1.000
ph
cdc
nm
ppm

FIG. 62

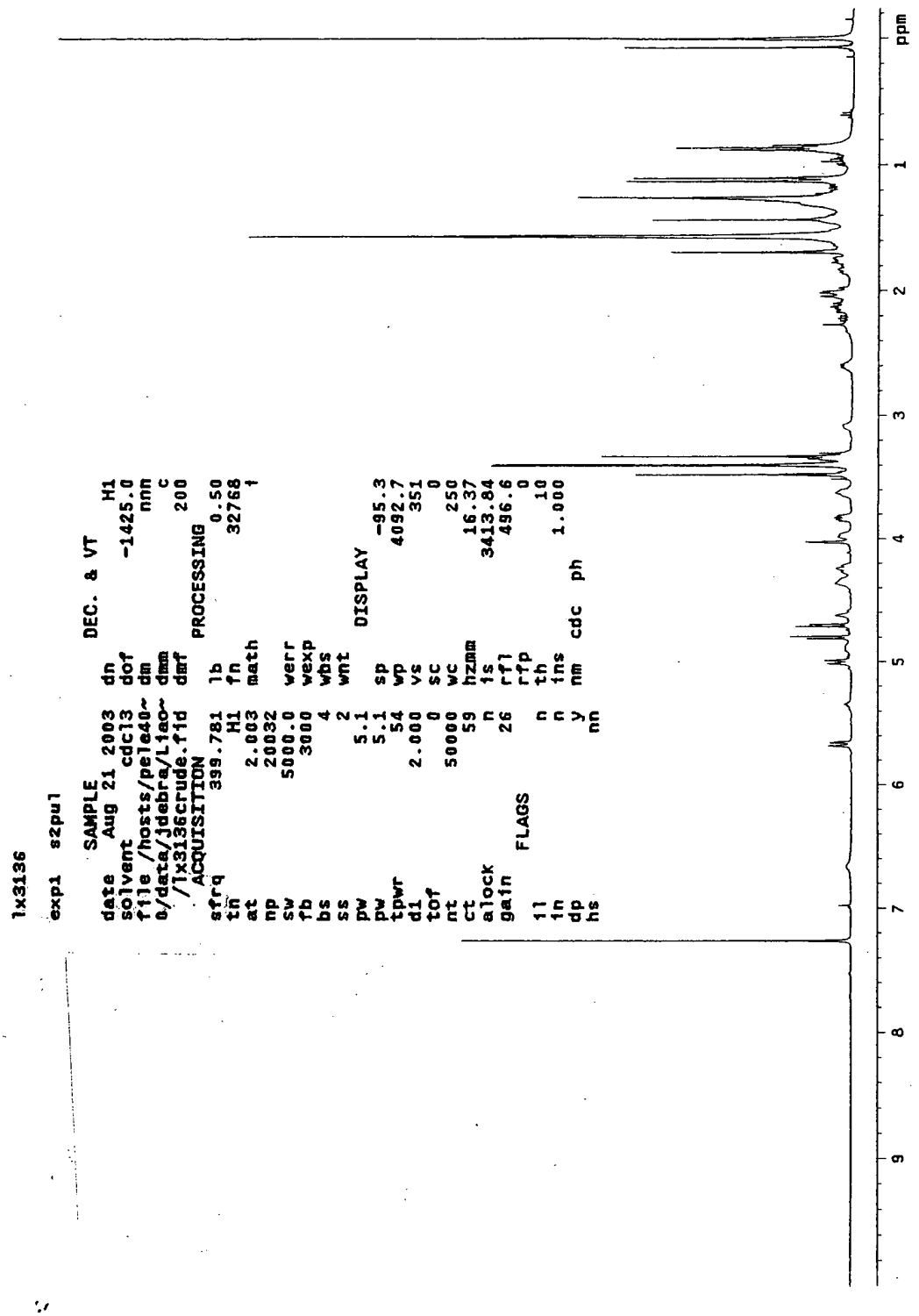

1x3136
exp1 s2pul
SAMPLE
date Aug 21 2003
solvent cdcl3
file /hosts/pele40~
d/data/jdebra/L1ao~
/1x3136crude.fid
ACQUISITION
sfrq 399.781
tn H1
at 2.003
np 20032
sw 5000.0
fb 3000
bs 4
ss 2
pw 5.1
pw 5.1
tpwr 54
d1 2.000
tof 0
nt 50000
ct 59
alock n
gain 26
FLAGS
il n
in n
dp y
hs nn
DEC. & VT
dn H1
dof -1425.0
dm nnn
dmm c
dmf 200
PROCESSING
lb 0.50
fn 32768
math f
werr
wexp
wbs
wnt
DISPLAY
sp -95.3
wp 4092.7
vs 351
sc 0
wc 250
hzmm 16.37
is 3413.84
rfl 496.6
rfp 0
th 10
ins 1.000
nm cdc ph
ppm

FIG. 63

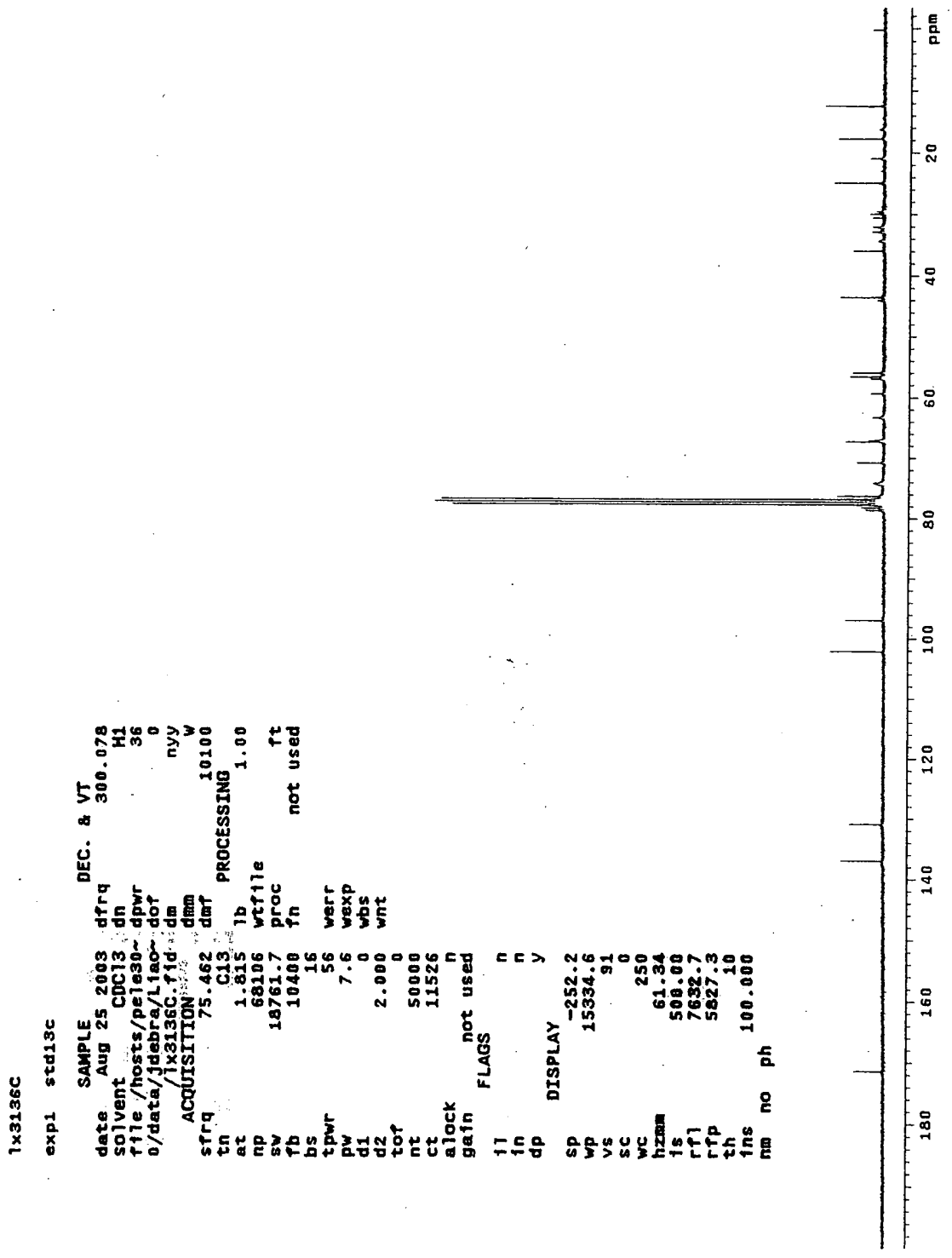

1x3136C
expl stdl3c
SAMPLE
date Aug 25 2003
solvent CDCl3
file /hosts/pele30~
o/data/jdebra/Liao~
/1x3136C.fid
ACQUISITION
sfrq 75.462
tn C13
at 1.815
np 68106
sw 18761.7
fb 10400
bs 16
tpwr 56
pw 7.6
d1 0
d2 2.000
tof 0
nt 50000
ct 11526
alock n
gain not used
FLAGS
il n
in n
dp y
DISPLAY
sp -252.2
wp 15334.6
vs 91
sc 0
wc 250
hzmm 61.34
is 508.00
rfl 7632.7
rfp 5827.3
th 10
ins 100.000
nm no ph
DEC. & VT
dfrq 300.078
dn H1
dpwr 36
dof 0
dm nyy
dmm w
dmf 10100
PROCESSING
lb 1.00
wtfile
proc ft
fn not used
werr
wexp
wbs
wnt
ppm
180
160
140
120
100
80
60
40
20

FIG. 64

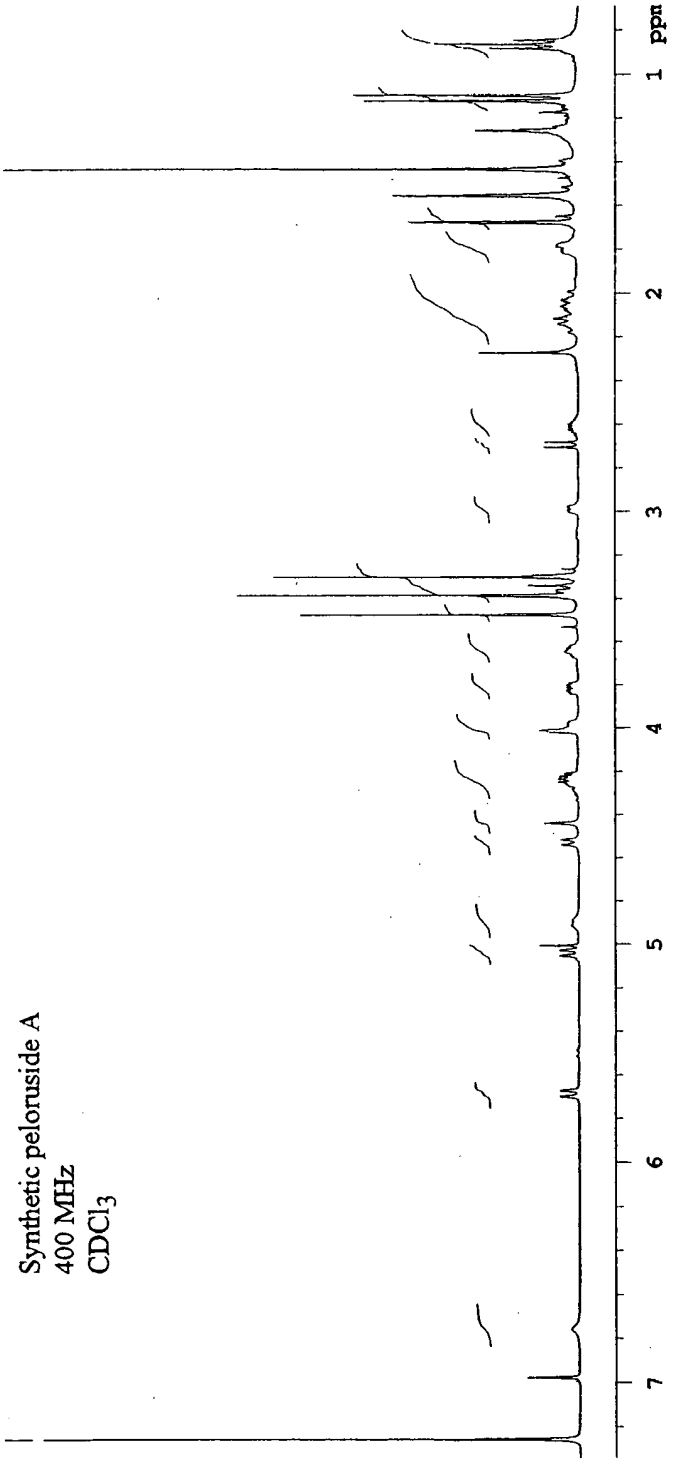


FIG. 65

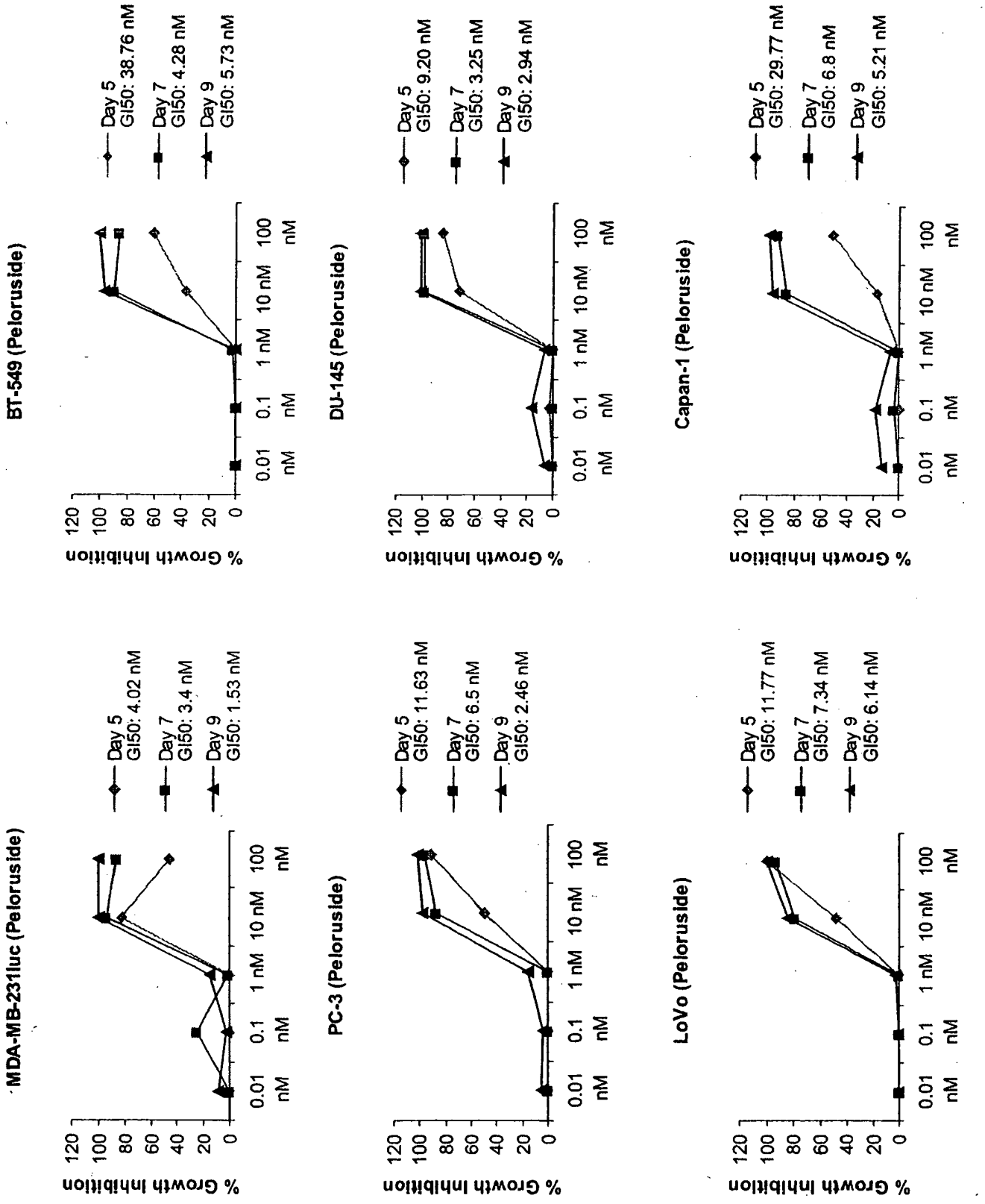

BT-549 (Peloruside)
Day 5 GI50: 38.76 nM
Day 7 GI50: 4.28 nM
Day 9 GI50: 5.73 nM
DU-145 (Peloruside)
Day 5 GI50: 9.20 nM
Day 7 GI50: 3.25 nM
Day 9 GI50: 2.94 nM
Capan-1 (Peloruside)
Day 5 GI50: 29.77 nM
Day 7 GI50: 6.8 nM
Day 9 GI50: 5.21 nM
MDA-MB-231luc (Peloruside)
Day 5 GI50: 4.02 nM
Day 7 GI50: 3.4 nM
Day 9 GI50: 1.53 nM
PC-3 (Peloruside)
Day 5 GI50: 11.63 nM
Day 7 GI50: 6.5 nM
Day 9 GI50: 2.46 nM
LoVo (Peloruside)
Day 5 GI50: 11.77 nM
Day 7 GI50: 7.34 nM
Day 9 GI50: 6.14 nM
% Growth Inhibition
0 20 40 60 80 100 120
0.01 nM 0.1 nM 1 nM 10 nM 100 nM

FIG. 66

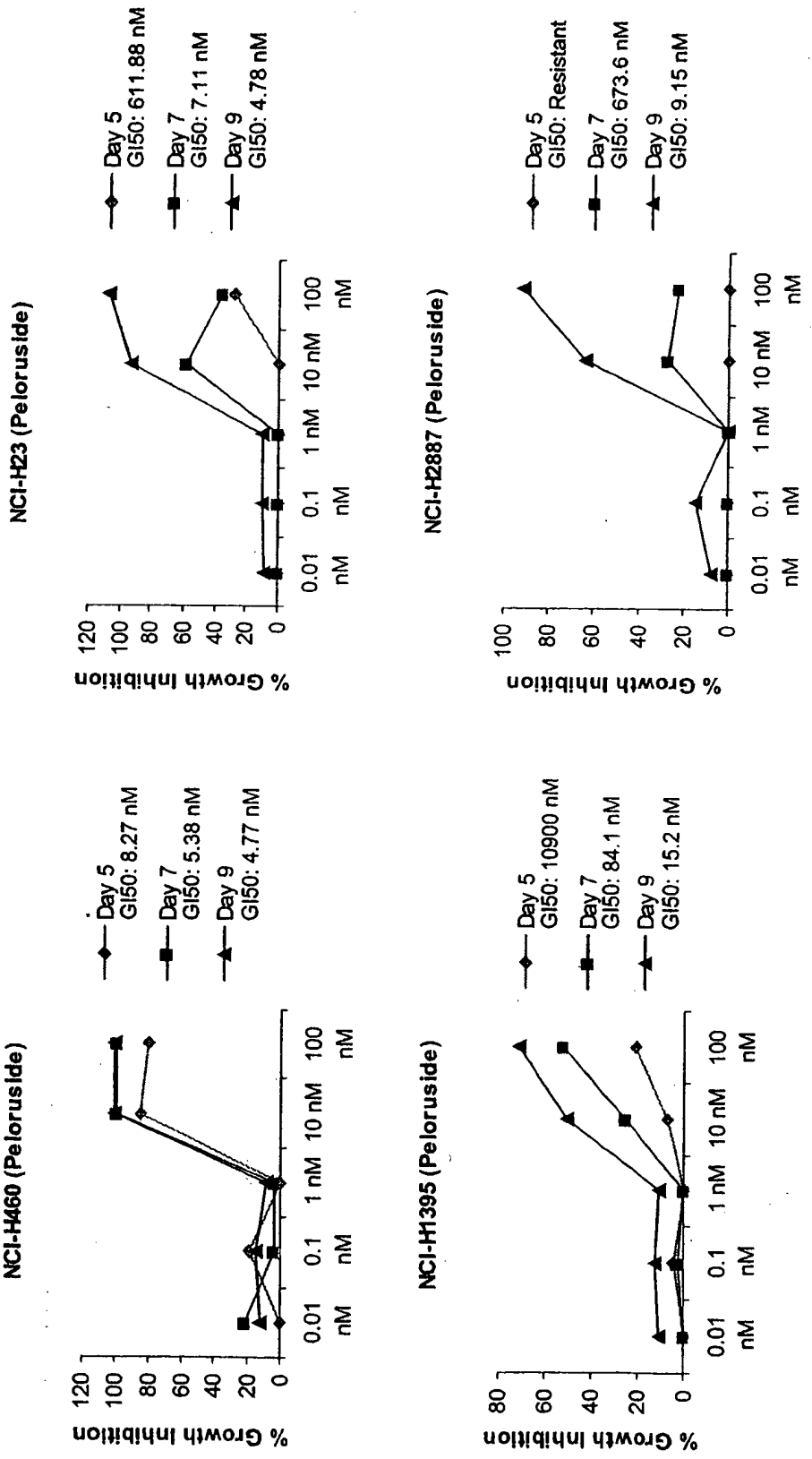

NCI-H23 (Peloruside)
Day 5 GI50: 611.88 nM
Day 7 GI50: 7.11 nM
Day 9 GI50: 4.78 nM
% Growth Inhibition
120
100
80
60
40
20
0
0.01 nM
0.1 nM
1 nM
10 nM
100 nM
NCI-H2887 (Peloruside)
Day 5 GI50: Resistant
Day 7 GI50: 673.6 nM
Day 9 GI50: 9.15 nM
% Growth Inhibition
100
80
60
40
20
0
0.01 nM
0.1 nM
1 nM
10 nM
100 nM
NCI-H460 (Peloruside)
Day 5 GI50: 8.27 nM
Day 7 GI50: 5.38 nM
Day 9 GI50: 4.77 nM
% Growth Inhibition
120
100
80
60
40
20
0
0.01 nM
0.1 nM
1 nM
10 nM
100 nM
NCI-H1395 (Peloruside)
Day 5 GI50: 10900 nM
Day 7 GI50: 84.1 nM
Day 9 GI50: 15.2 nM
% Growth Inhibition
80
60
40
20
0
0.01 nM
0.1 nM
1 nM
10 nM
100 nM

FIG. 67

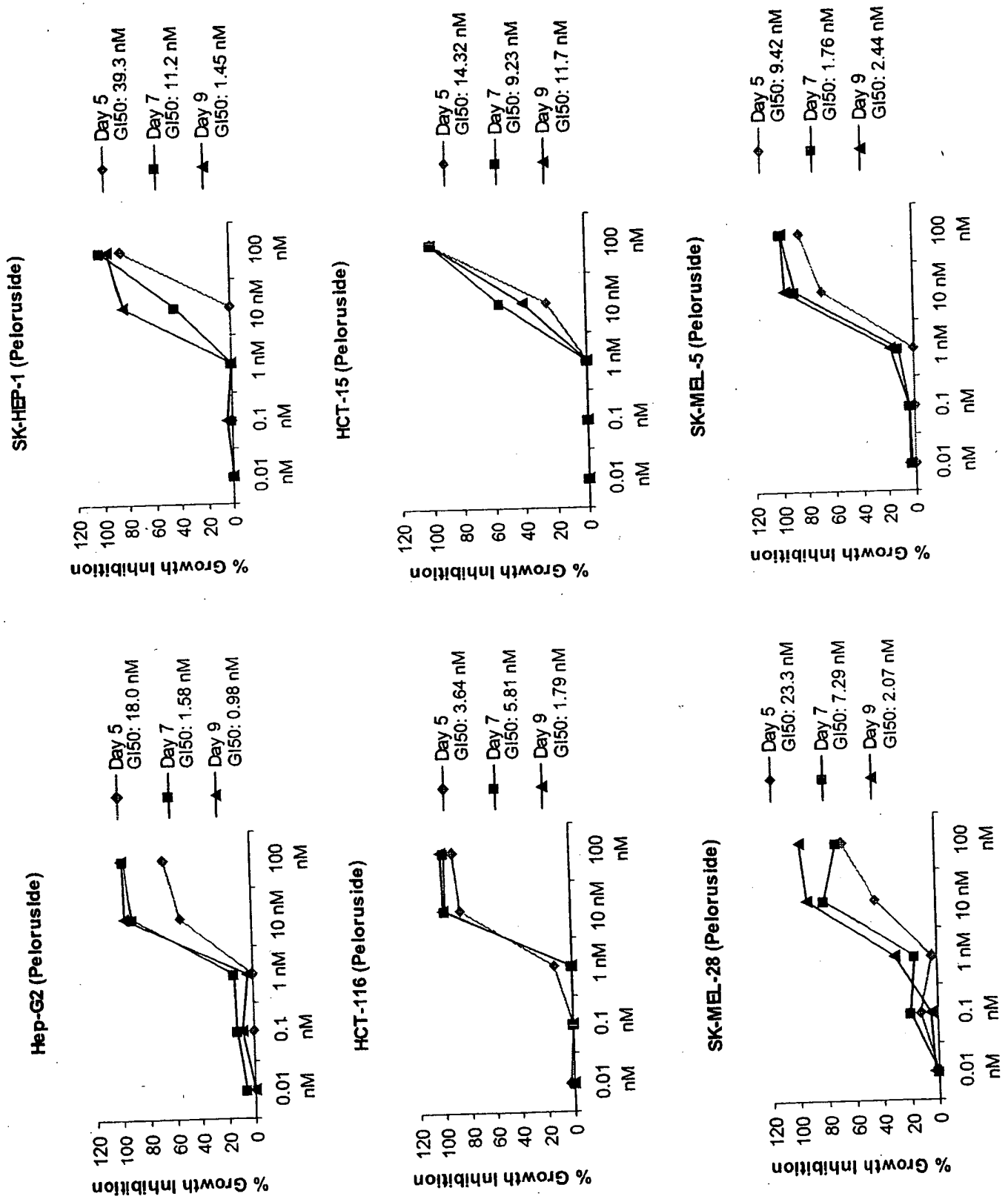

SK-HEP-1 (Peloruside)
Day 5 GI50: 39.3 nM
Day 7 GI50: 11.2 nM
Day 9 GI50: 1.45 nM
% Growth Inhibition
HCT-15 (Peloruside)
Day 5 GI50: 14.32 nM
Day 7 GI50: 9.23 nM
Day 9 GI50: 11.7 nM
SK-MEL-5 (Peloruside)
Day 5 GI50: 9.42 nM
Day 7 GI50: 1.76 nM
Day 9 GI50: 2.44 nM
Hep-G2 (Peloruside)
Day 5 GI50: 18.0 nM
Day 7 GI50: 1.58 nM
Day 9 GI50: 0.98 nM
HCT-116 (Peloruside)
Day 5 GI50: 3.64 nM
Day 7 GI50: 5.81 nM
Day 9 GI50: 1.79 nM
SK-MEL-28 (Peloruside)
Day 5 GI50: 23.3 nM
Day 7 GI50: 7.29 nM
Day 9 GI50: 2.07 nM
0 20 40 60 80 100 120
0.01 nM 0.1 nM 1 nM 10 nM 100 nM

FIG. 68

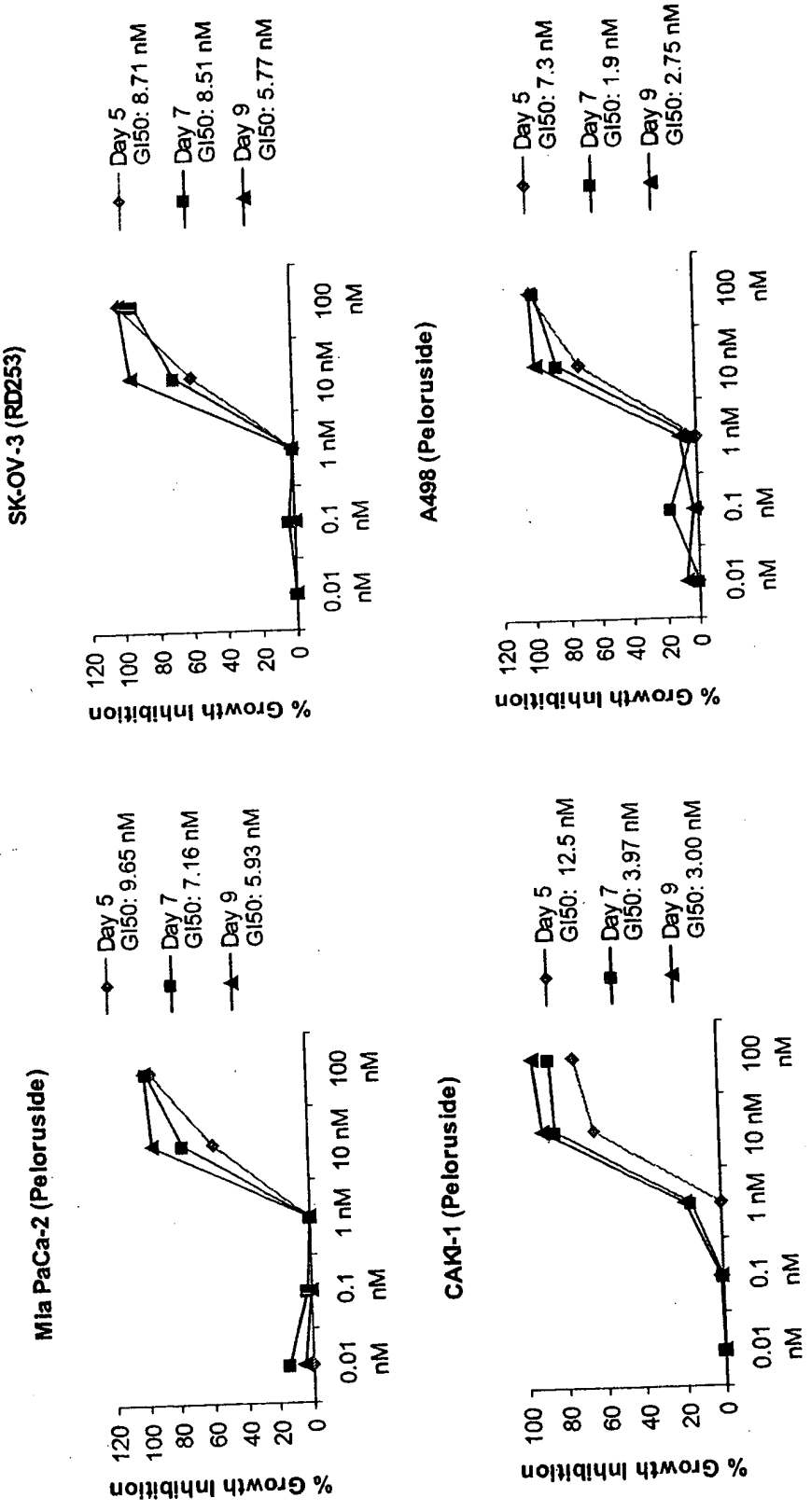

SK-OV-3 (RD253)
Day 5 GI50: 8.71 nM
Day 7 GI50: 8.51 nM
Day 9 GI50: 5.77 nM
% Growth Inhibition
120
100
80
60
40
20
0
0.01 nM
0.1 nM
1 nM
10 nM
100 nM
A498 (Peloruside)
Day 5 GI50: 7.3 nM
Day 7 GI50: 1.9 nM
Day 9 GI50: 2.75 nM
Mia PaCa-2 (Peloruside)
Day 5 GI50: 9.65 nM
Day 7 GI50: 7.16 nM
Day 9 GI50: 5.93 nM
CAKI-1 (Peloruside)
Day 5 GI50: 12.5 nM
Day 7 GI50: 3.97 nM
Day 9 GI50: 3.00 nM

FIG. 69

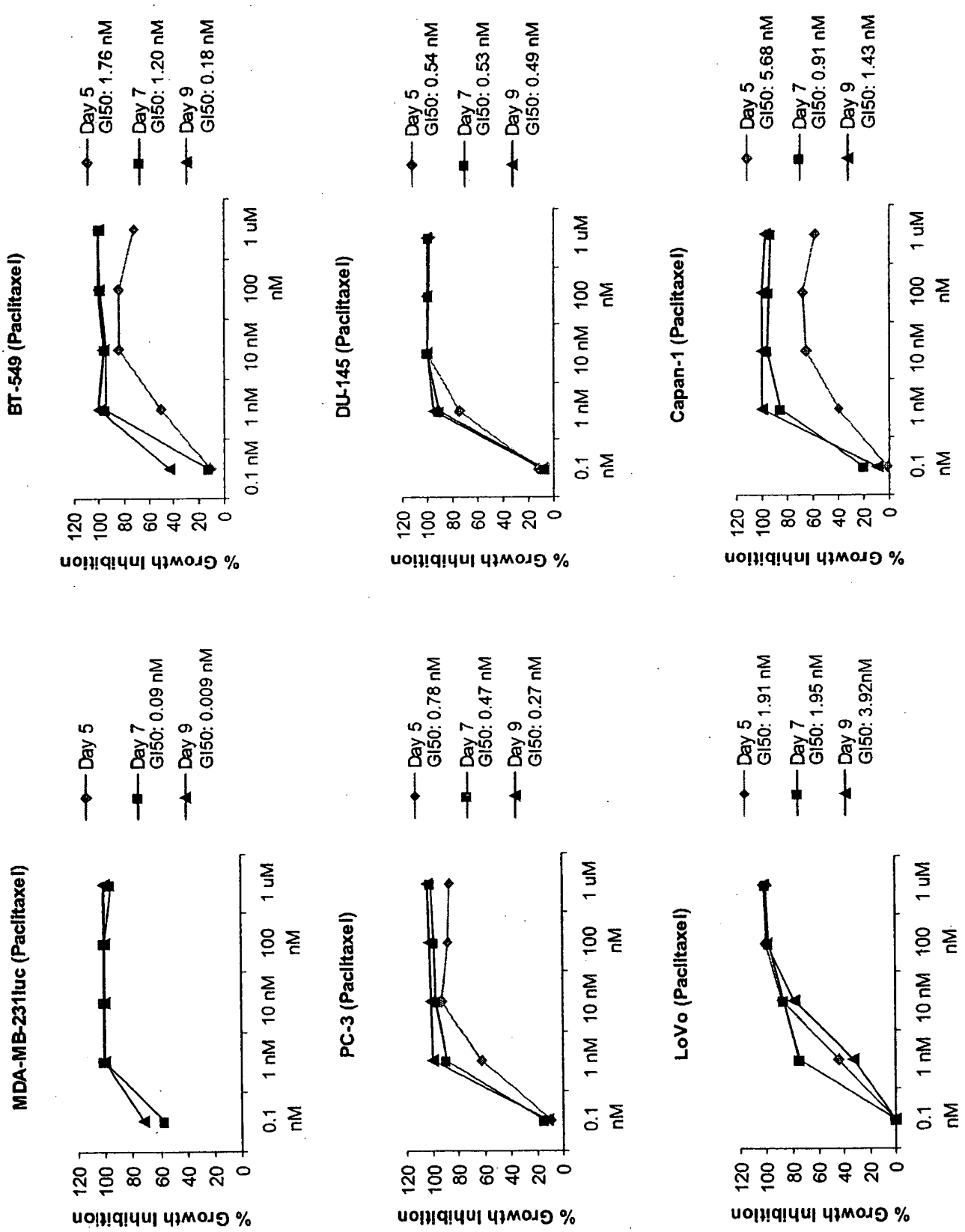

BT-549 (Paclitaxel)
Day 5 GI50: 1.76 nM
Day 7 GI50: 1.20 nM
Day 9 GI50: 0.18 nM
% Growth Inhibition
0.1 nM 1 nM 10 nM 100 nM 1 uM
DU-145 (Paclitaxel)
Day 5 GI50: 0.54 nM
Day 7 GI50: 0.53 nM
Day 9 GI50: 0.49 nM
Capan-1 (Paclitaxel)
Day 5 GI50: 5.68 nM
Day 7 GI50: 0.91 nM
Day 9 GI50: 1.43 nM
MDA-MB-231luc (Paclitaxel)
Day 5
Day 7 GI50: 0.09 nM
Day 9 GI50: 0.009 nM
PC-3 (Paclitaxel)
Day 5 GI50: 0.78 nM
Day 7 GI50: 0.47 nM
Day 9 GI50: 0.27 nM
LoVo (Paclitaxel)
Day 5 GI50: 1.91 nM
Day 7 GI50: 1.95 nM
Day 9 GI50: 3.92nM

FIG. 70

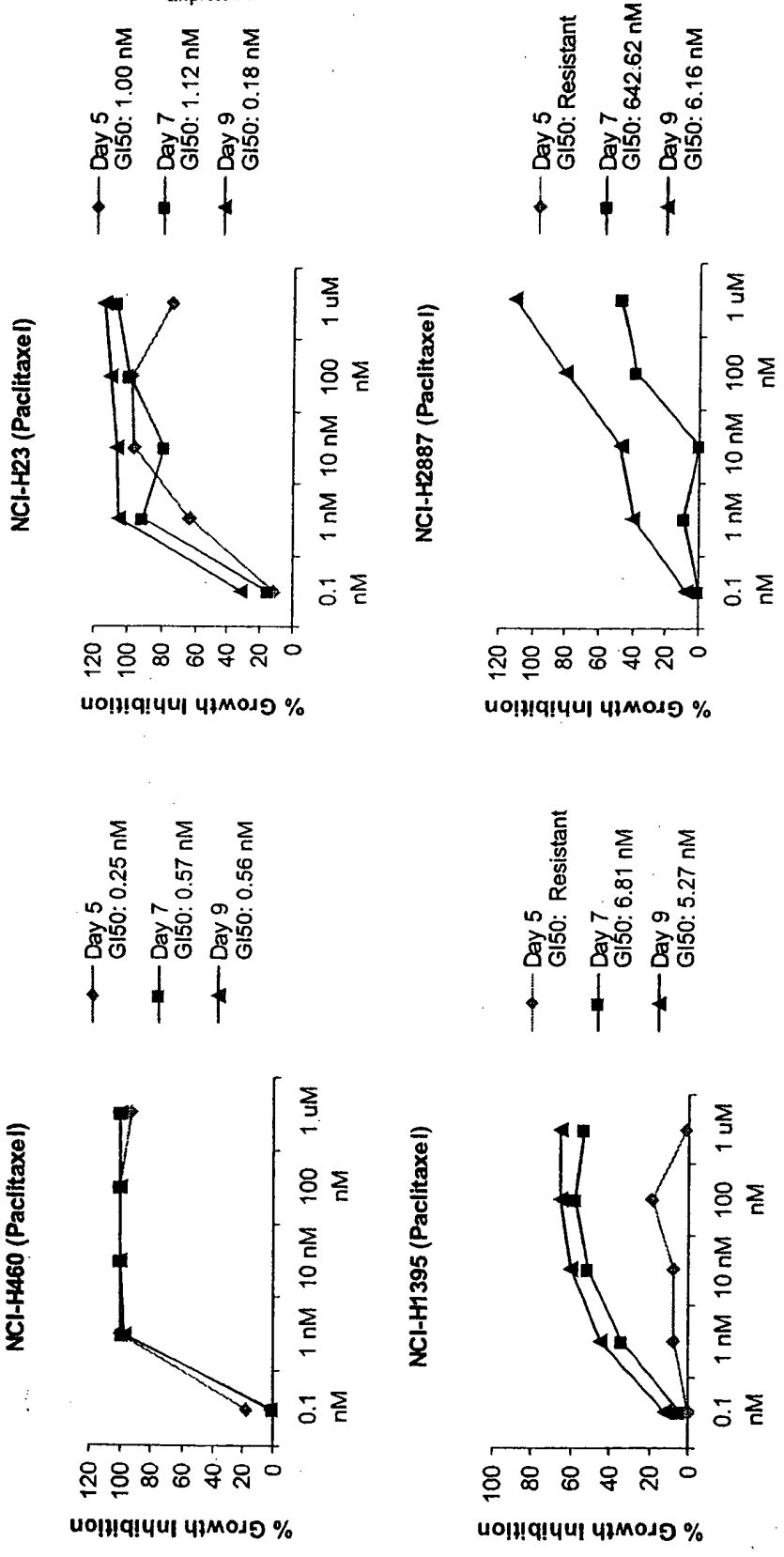

NCI-H23 (Paclitaxel)
Day 5 GI50: 1.00 nM
Day 7 GI50: 1.12 nM
Day 9 GI50: 0.18 nM
% Growth Inhibition
0 20 40 60 80 100 120
0.1 nM 1 nM 10 nM 100 nM 1 uM
NCI-H2887 (Paclitaxel)
Day 5 GI50: Resistant
Day 7 GI50: 642.62 nM
Day 9 GI50: 6.16 nM
% Growth Inhibition
0 20 40 60 80 100 120
0.1 nM 1 nM 10 nM 100 nM 1 uM
NCI-H460 (Paclitaxel)
Day 5 GI50: 0.25 nM
Day 7 GI50: 0.57 nM
Day 9 GI50: 0.56 nM
% Growth Inhibition
0 20 40 60 80 100 120
0.1 nM 1 nM 10 nM 100 nM 1 uM
NCI-H1395 (Paclitaxel)
Day 5 GI50: Resistant
Day 7 GI50: 6.81 nM
Day 9 GI50: 5.27 nM
% Growth Inhibition
0 20 40 60 80 100
0.1 nM 1 nM 10 nM 100 nM 1 uM

FIG. 71

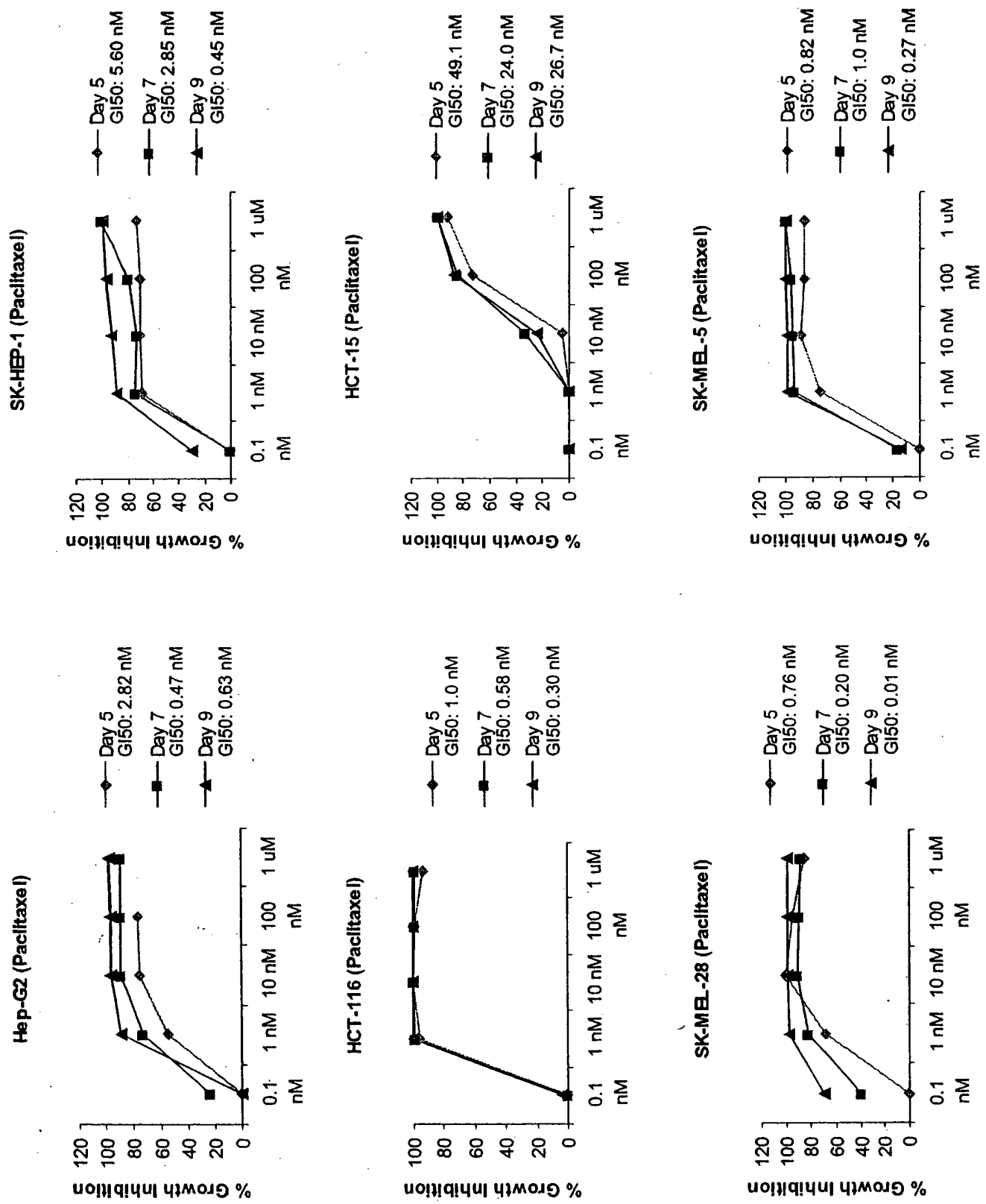

SK-HEP-1 (Paclitaxel)
Day 5 GI50: 5.60 nM
Day 7 GI50: 2.85 nM
Day 9 GI50: 0.45 nM
HCT-15 (Paclitaxel)
Day 5 GI50: 49.1 nM
Day 7 GI50: 24.0 nM
Day 9 GI50: 26.7 nM
SK-MEL-5 (Paclitaxel)
Day 5 GI50: 0.82 nM
Day 7 GI50: 1.0 nM
Day 9 GI50: 0.27 nM
Hep-G2 (Paclitaxel)
Day 5 GI50: 2.82 nM
Day 7 GI50: 0.47 nM
Day 9 GI50: 0.63 nM
HCT-116 (Paclitaxel)
Day 5 GI50: 1.0 nM
Day 7 GI50: 0.58 nM
Day 9 GI50: 0.30 nM
SK-MEL-28 (Paclitaxel)
Day 5 GI50: 0.76 nM
Day 7 GI50: 0.20 nM
Day 9 GI50: 0.01 nM
% Growth Inhibition
0 20 40 60 80 100 120
0.1 nM 1 nM 10 nM 100 nM 1 uM

FIG. 72

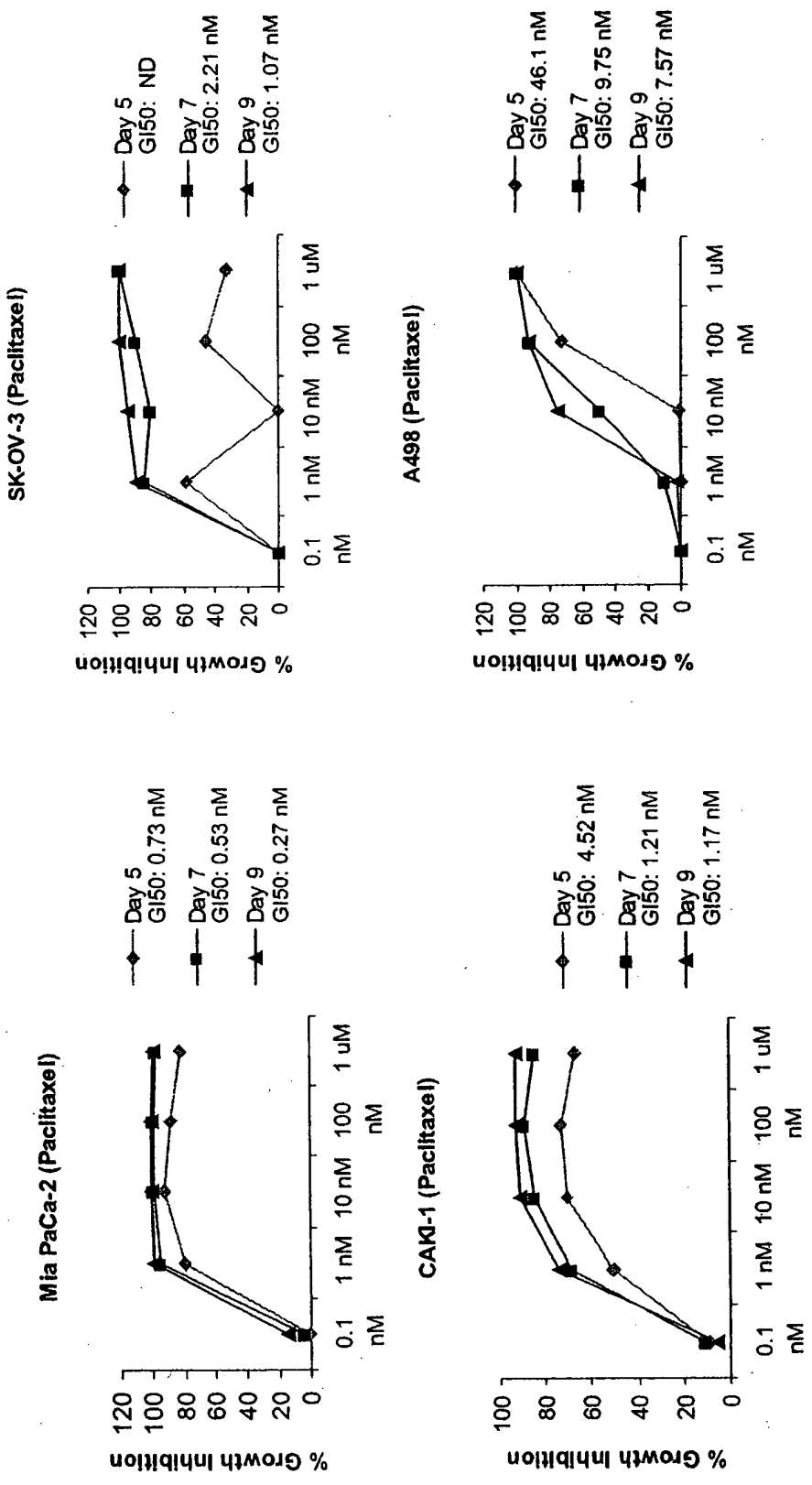
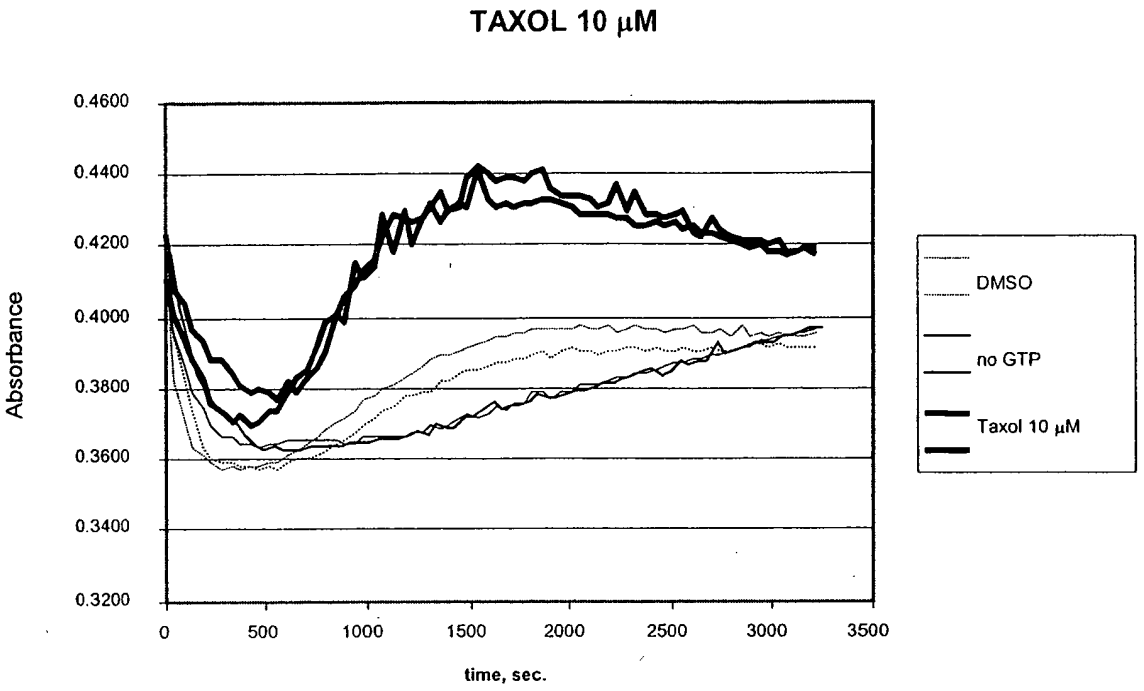

SK-OV-3 (Paclitaxel)
Day 5 GI50: ND
Day 7 GI50: 2.21 nM
Day 9 GI50: 1.07 nM
% Growth Inhibition
0.1 nM 1 nM 10 nM 100 nM 1 uM
A498 (Paclitaxel)
Day 5 GI50: 46.1 nM
Day 7 GI50: 9.75 nM
Day 9 GI50: 7.57 nM
Mia PaCa-2 (Paclitaxel)
Day 5 GI50: 0.73 nM
Day 7 GI50: 0.53 nM
Day 9 GI50: 0.27 nM
CAKI-1 (Paclitaxel)
Day 5 GI50: 4.52 nM
Day 7 GI50: 1.21 nM
Day 9 GI50: 1.17 nM

FIG. 73


TAXOL 10 μM
Absorbance
0.4600
0.4400
0.4200
0.4000
0.3800
0.3600
0.3400
0.3200
0
500
1000
1500
2000
2500
3000
3500
time, sec.
DMSO
no GTP
Taxol 10 μM

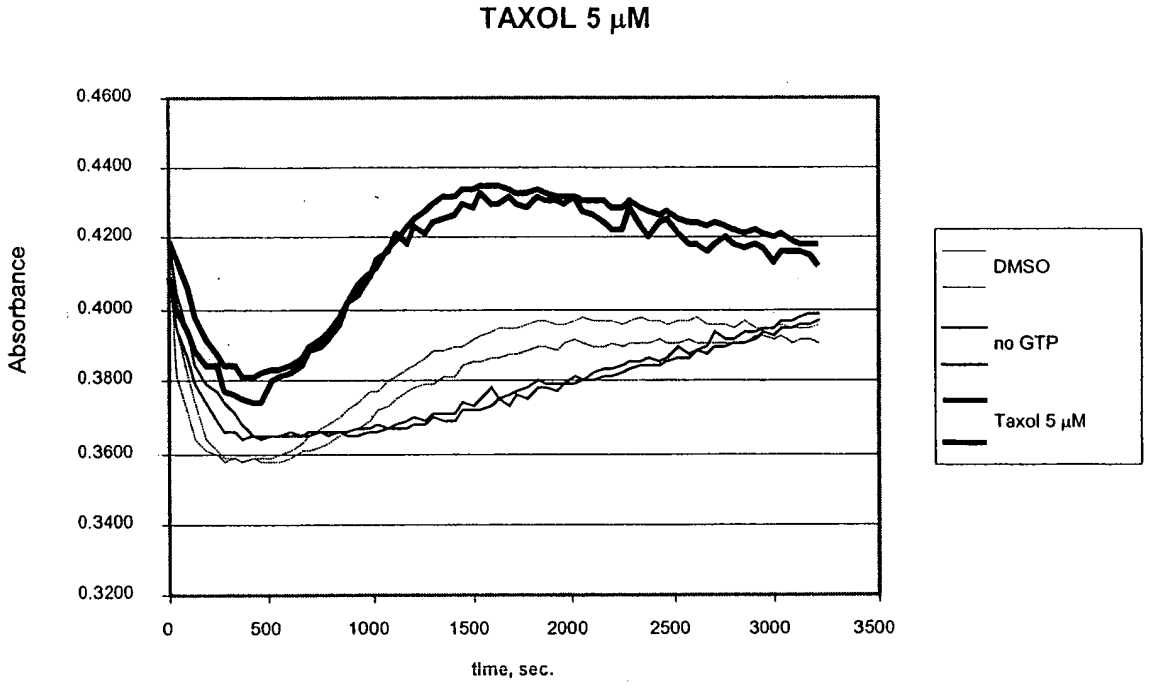
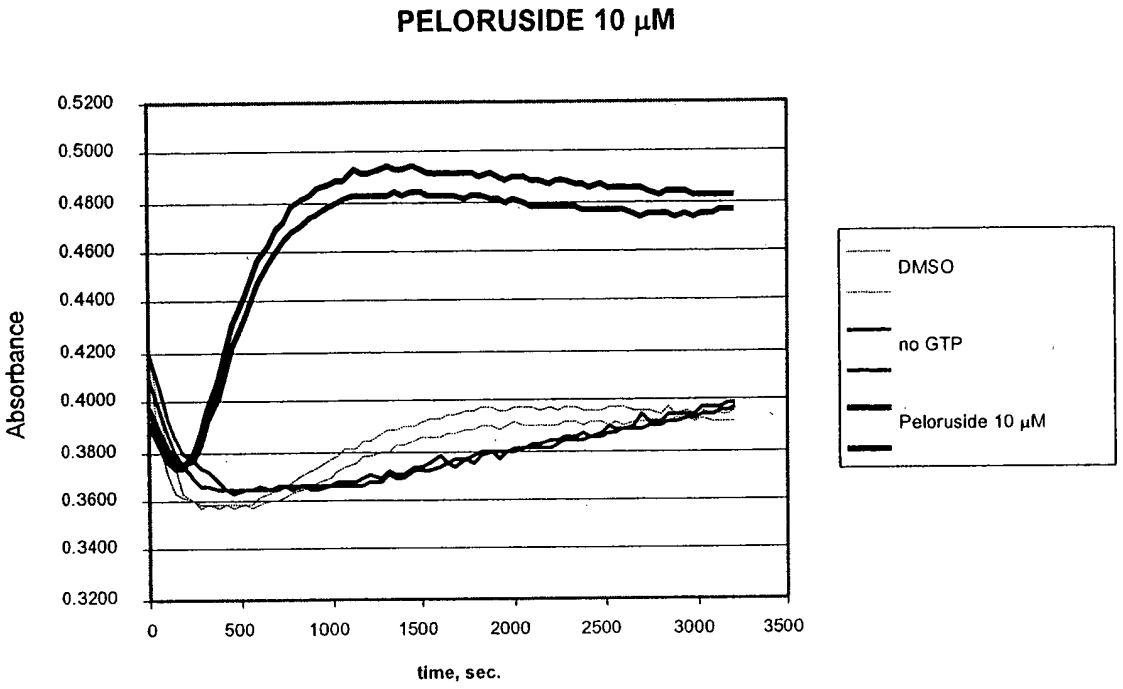

TAXOL 5 μM
Absorbance
0.4600
0.4400
0.4200
0.4000
0.3800
0.3600
0.3400
0.3200
0
500
1000
1500
2000
2500
3000
3500
time, sec.
DMSO
no GTP
Taxol 5 μM

FIG. 74


PELORUSIDE 10 μM
Absorbance
0.5200
0.5000
0.4800
0.4600
0.4400
0.4200
0.4000
0.3800
0.3600
0.3400
0.3200
0
500
1000
1500
2000
2500
3000
3500
time, sec.
DMSO
no GTP
Peloruside 10 μM

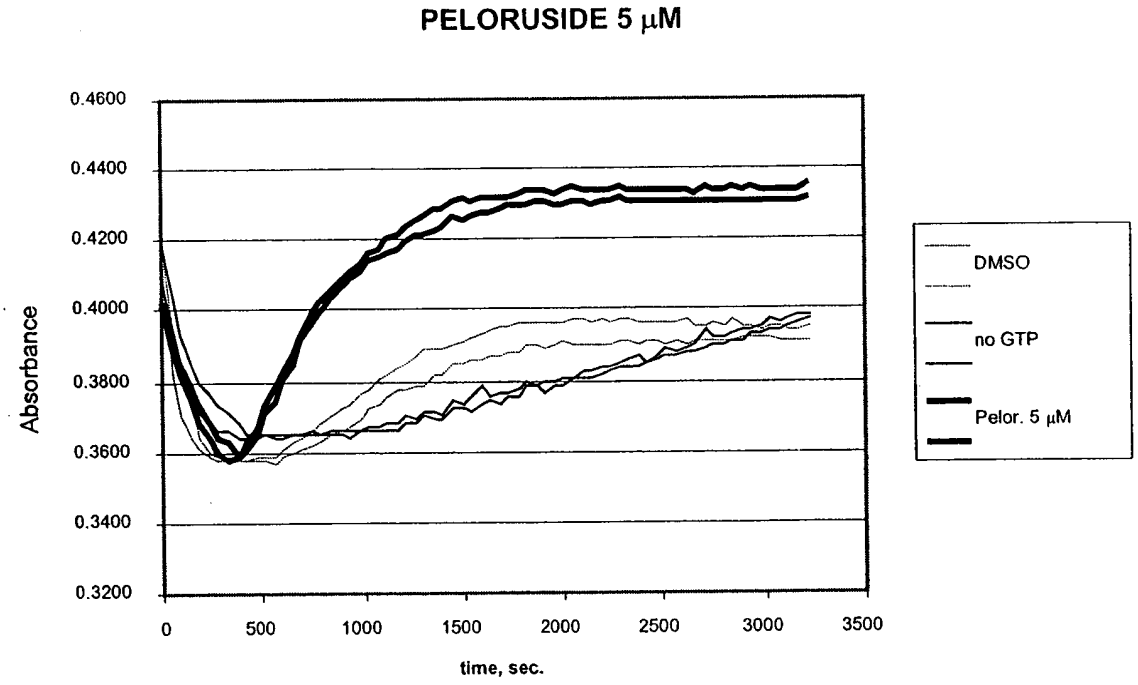
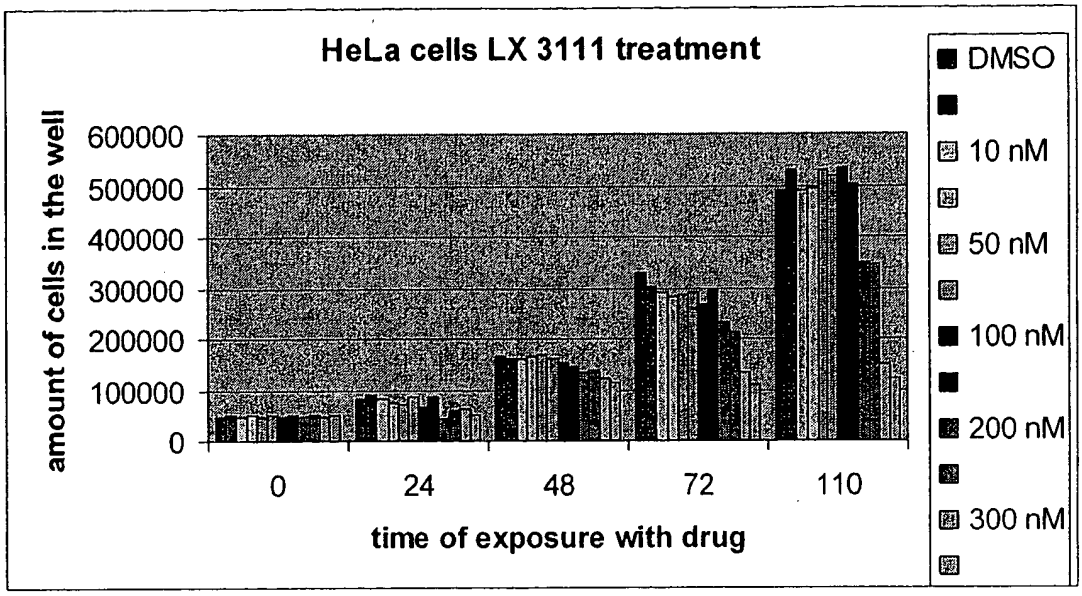

PELORUSIDE 5 μM
Absorbance
0.4600
0.4400
0.4200
0.4000
0.3800
0.3600
0.3400
0.3200
0
500
1000
1500
2000
2500
3000
3500
time, sec.
DMSO
no GTP
Pelor. 5 μM

FIG. 75

A


HeLa cells LX 3111 treatment
amount of cells in the well
600000
500000
400000
300000
200000
100000
0
0
24
48
72
110
time of exposure with drug
DMSO
10 nM
50 nM
100 nM
200 nM
300 nM

B

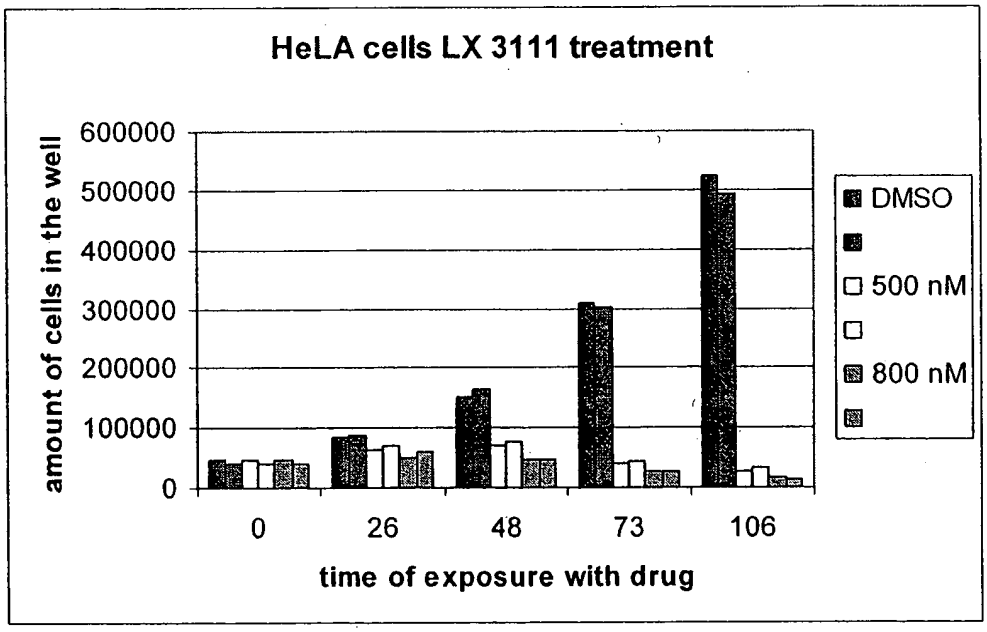

HeLA cells LX 3111 treatment
amount of cells in the well
600000
500000
400000
300000
200000
100000
0
0
26
48
73
106
time of exposure with drug
DMSO
500 nM
800 nM

FIG. 76

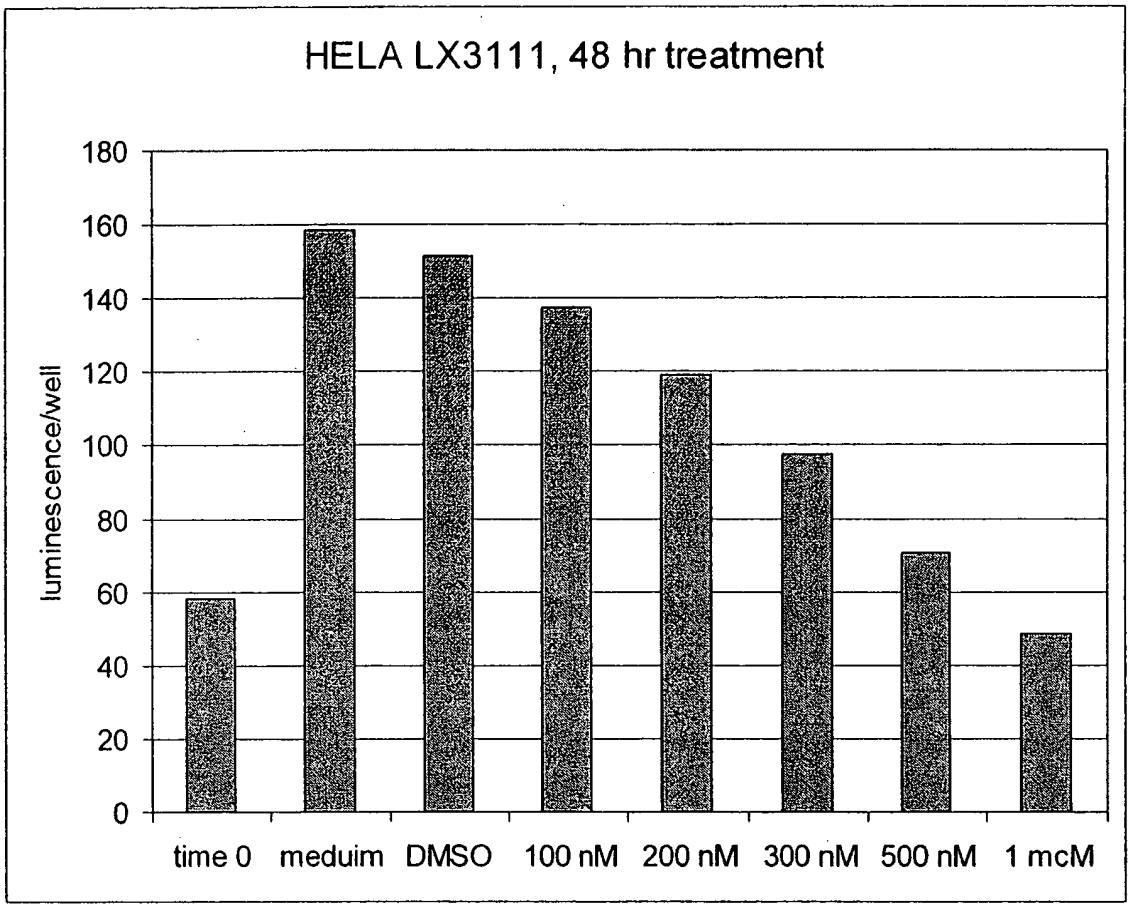
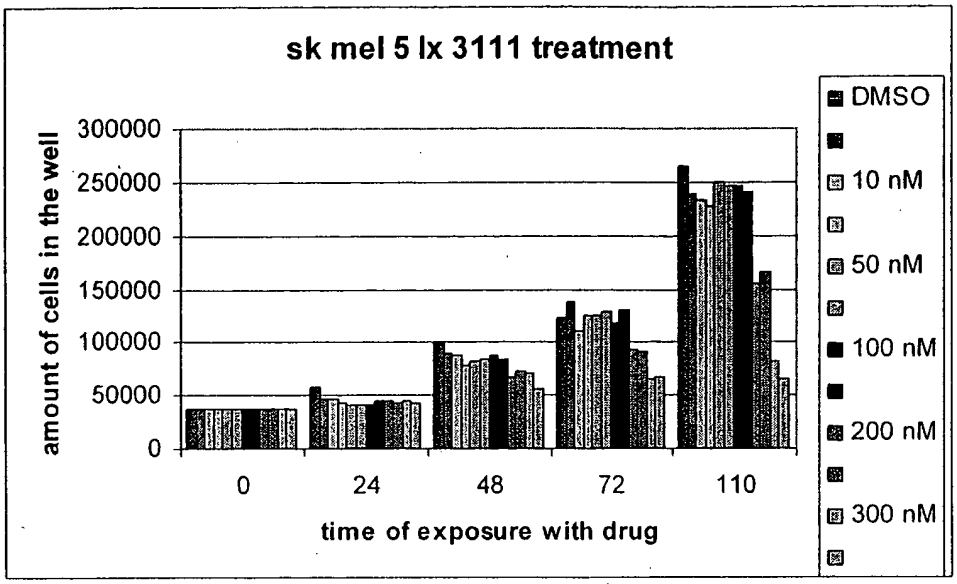

HELA LX3111, 48 hr treatment
luminescence/well
180
160
140
120
100
80
60
40
20
0
time 0
meduim
DMSO
100 nM
200 nM
300 nM
500 nM
1 mcM

FIG. 77

A


sk mel 5 lx 3111 treatment
amount of cells in the well
300000
250000
200000
150000
100000
50000
0
0
24
48
72
110
time of exposure with drug
DMSO
10 nM
50 nM
100 nM
200 nM
300 nM

B

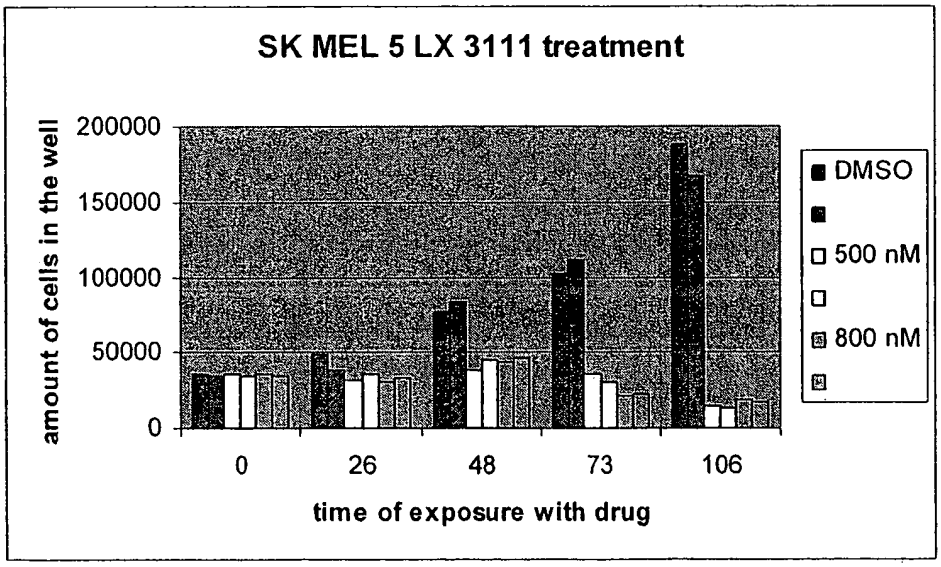

SK MEL 5 LX 3111 treatment
amount of cells in the well
200000
150000
100000
50000
0
0
26
48
73
106
time of exposure with drug
DMSO
500 nM
800 nM

FIG. 78

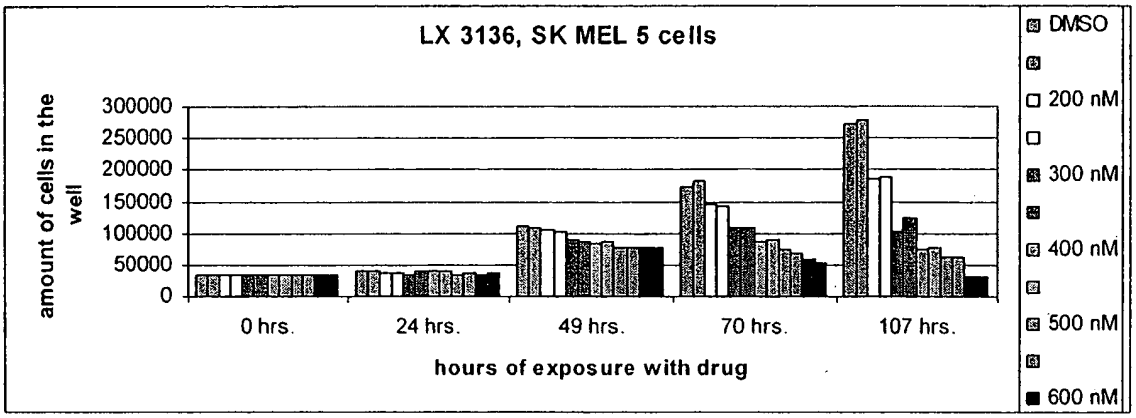
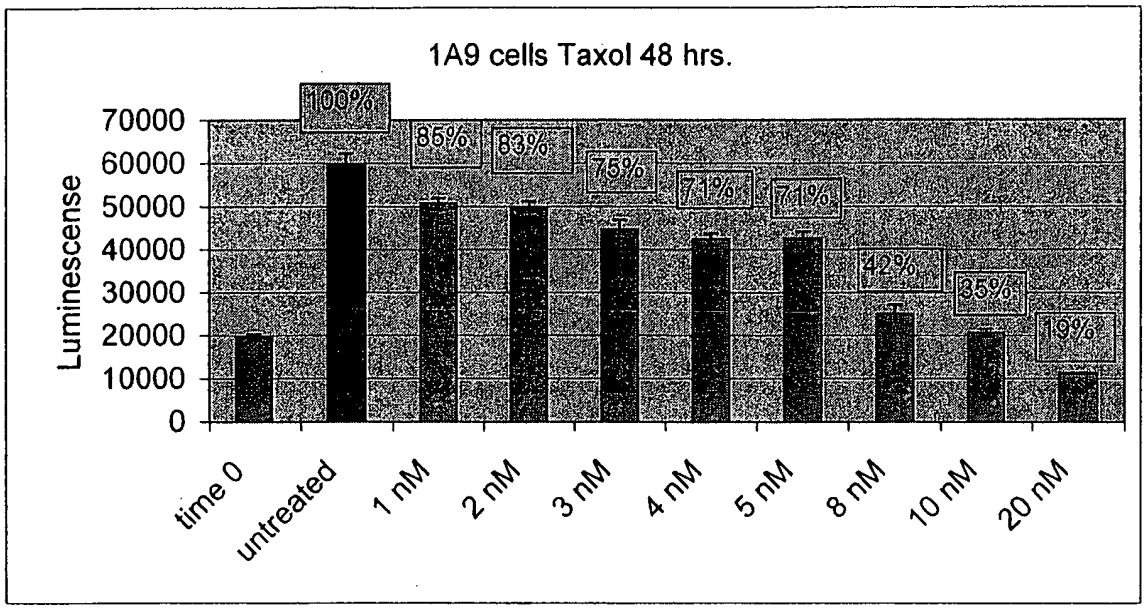
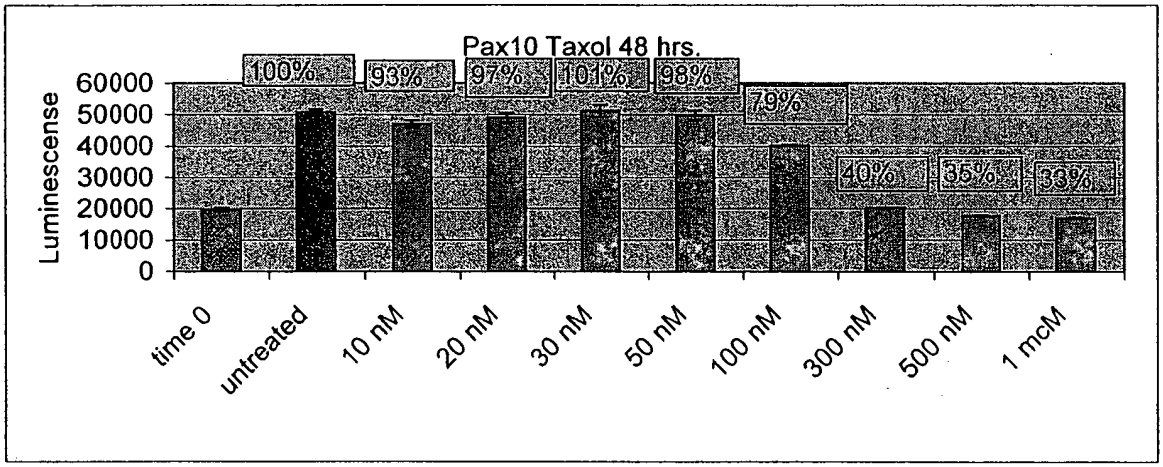

LX 3136, SK MEL 5 cells
amount of cells in the well
300000
250000
200000
150000
100000
50000
0
0 hrs.
24 hrs.
49 hrs.
70 hrs.
107 hrs.
hours of exposure with drug
DMSO
200 nM
300 nM
400 nM
500 nM
600 nM

FIG. 79


1A9 cells Taxol 48 hrs.
Luminescense
70000
60000
50000
40000
30000
20000
10000
0
100%
85%
83%
75%
71%
71%
42%
35%
19%
time 0
untreated
1 nM
2 nM
3 nM
4 nM
5 nM
8 nM
10 nM
20 nM


Pax10 Taxol 48 hrs.
Luminescense
60000
50000
40000
30000
20000
10000
0
100%
93%
97%
101%
98%
79%
40%
35%
33%
time 0
untreated
10 nM
20 nM
30 nM
50 nM
100 nM
300 nM
500 nM
1 mcM

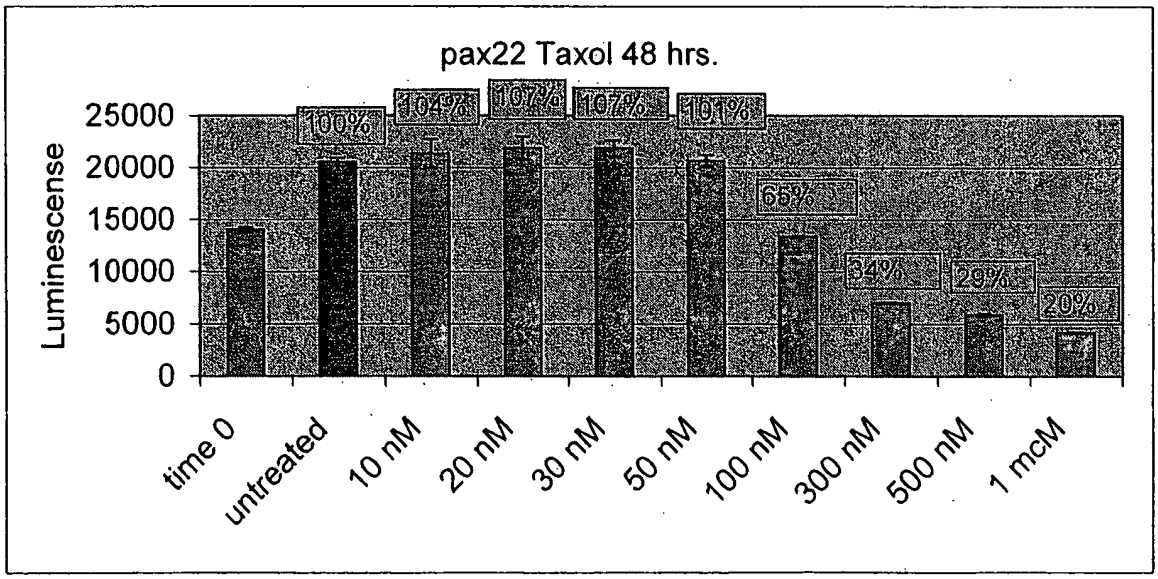
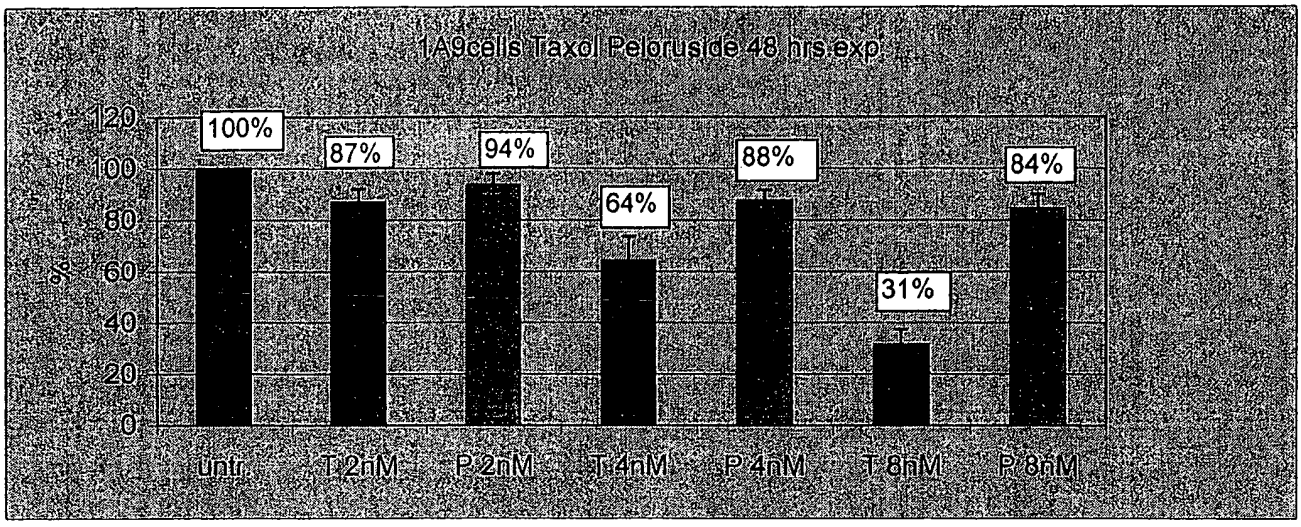
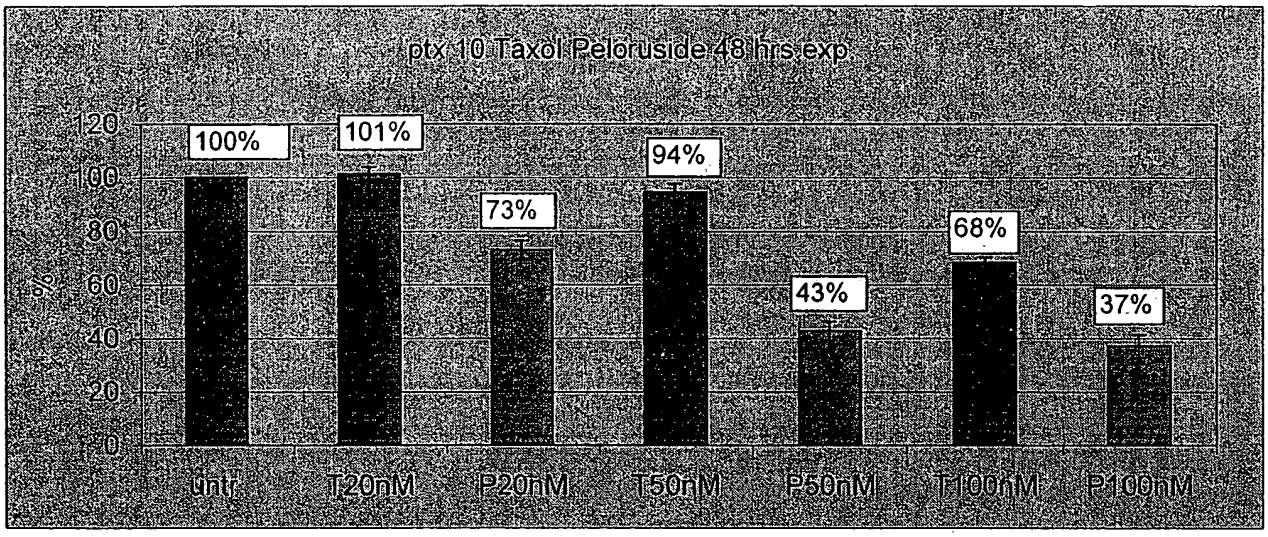

pax22 Taxol 48 hrs.
Luminescense
25000
20000
15000
10000
5000
0
100%
104%
107%
107%
101%
65%
34%
29%
20%
time 0
untreated
10 nM
20 nM
30 nM
50 nM
100 nM
300 nM
500 nM
1 mcM

FIG. 80


1A9cells Taxol Peloruside 48 hrs exp
120
100
80
60
40
20
0
100%
87%
94%
64%
88%
31%
84%
untr
T 2nM
P 2nM
T 4nM
P 4nM
T 8nM
P 8nM


ptx 10 Taxol Peloruside 48 hrs exp
120
100
80
60
40
20
0
100%
101%
73%
94%
43%
68%
37%
untr
T20nM
P20nM
T50nM
P50nM
T100nM
P100nM

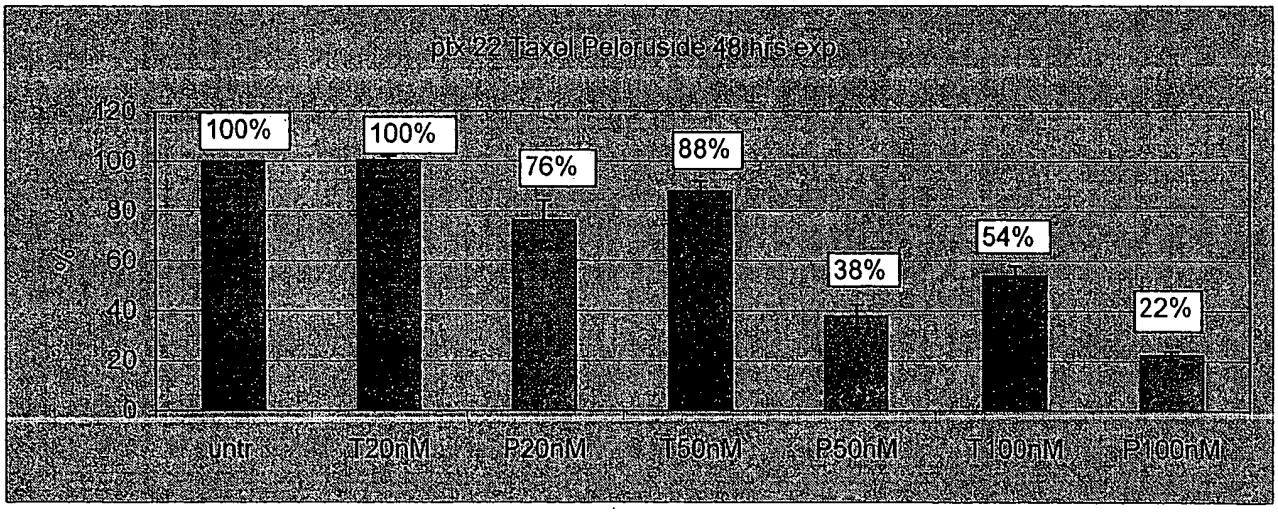
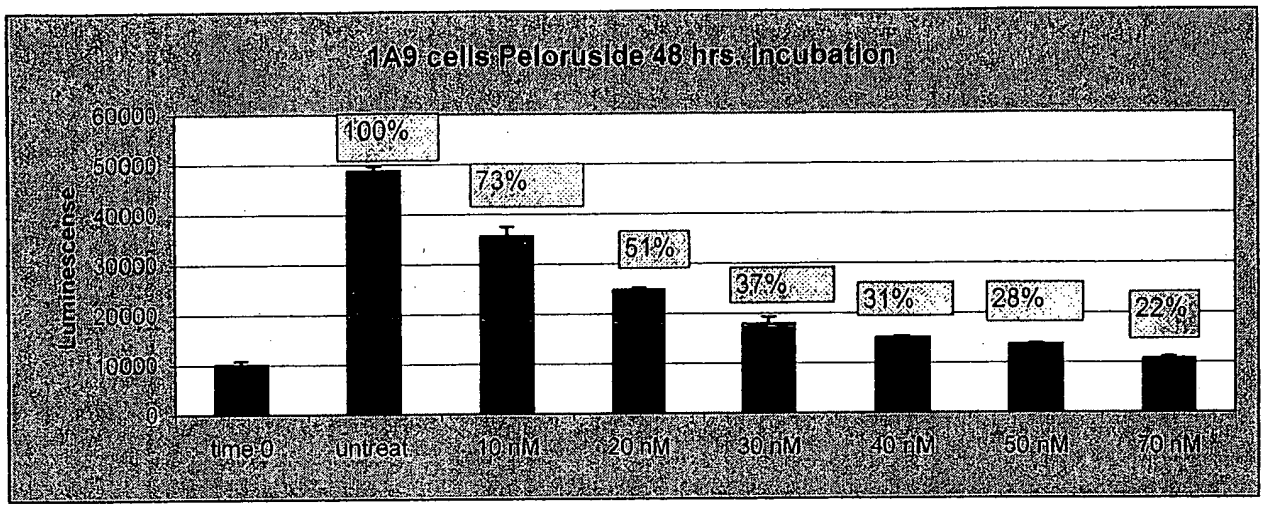
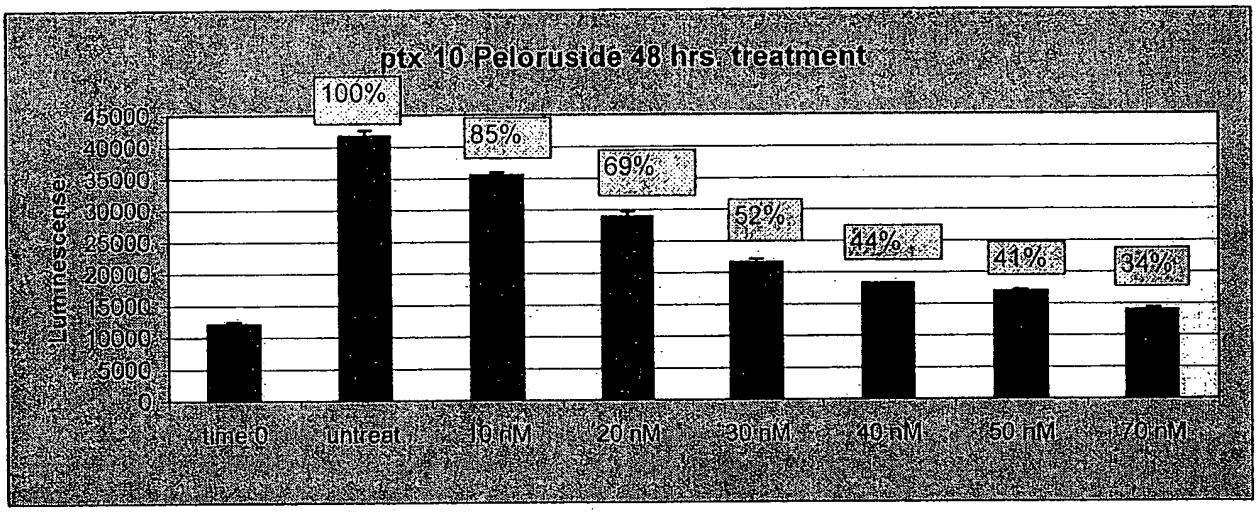

ptx 22 Taxol Peloruside 48 hrs exp
120
100
80
60
40
20
0
100%
100%
76%
88%
38%
54%
22%
untr
T20nM
P20nM
T50nM
P50nM
T100nM
P100nM

FIG. 81


1A9 cells Peloruside 48 hrs. Incubation
Luminescense
60000
50000
40000
30000
20000
10000
0
100%
73%
51%
37%
31%
28%
22%
time 0
untreat
10 nM
20 nM
30 nM
40 nM
50 nM
70 nM


ptx 10 Peloruside 48 hrs. treatment
Luminescense
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
100%
85%
69%
52%
44%
41%
34%
time 0
untreat
10 nM
20 nM
30 nM
40 nM
50 nM
70 nM

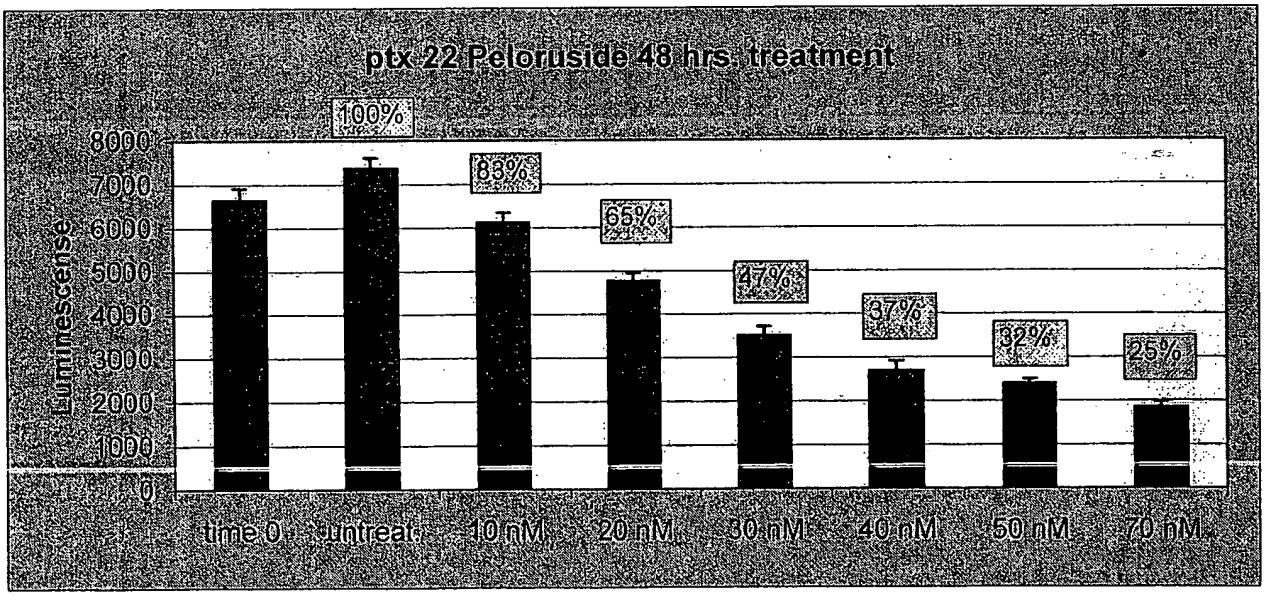

ptx 22 Peloruside 48 hrs. treatment
Luminescense
8000
7000
6000
5000
4000
3000
2000
1000
0
100%
83%
65%
47%
37%
32%
25%
time 0
untreat
10 nM
20 nM
30 nM
40 nM
50 nM
70 nM

FIG. 82

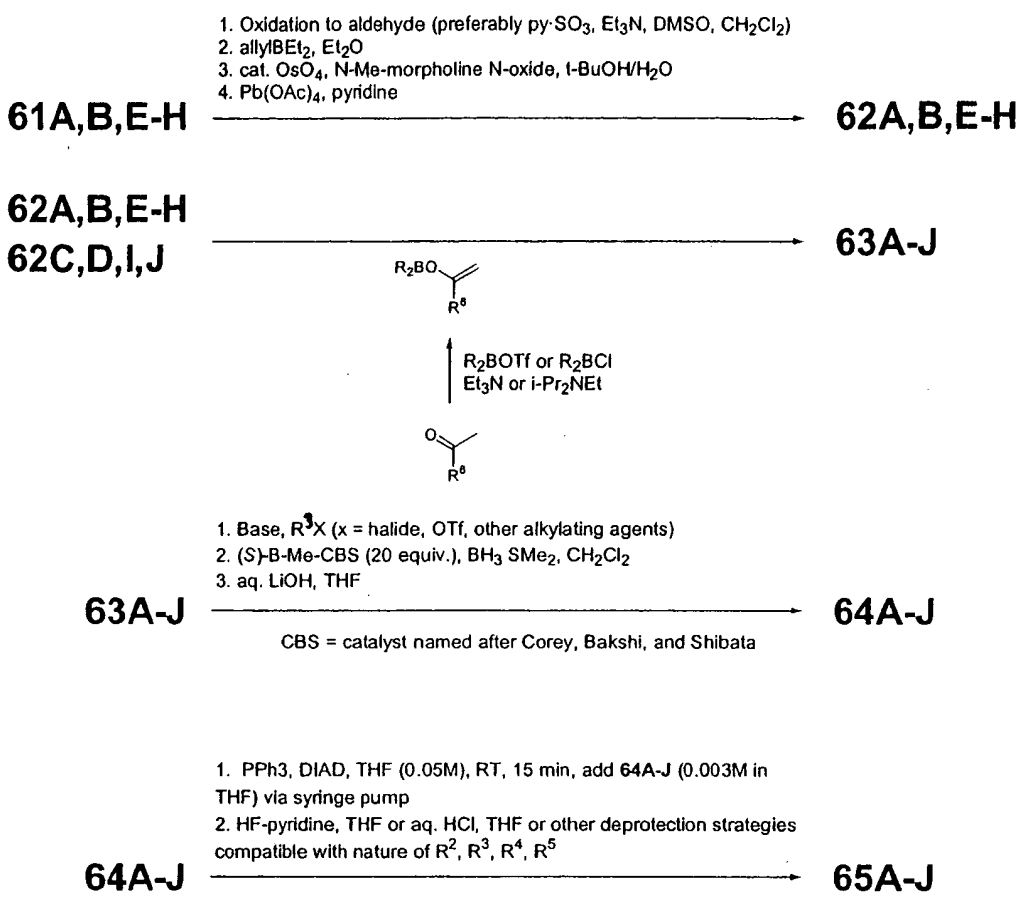
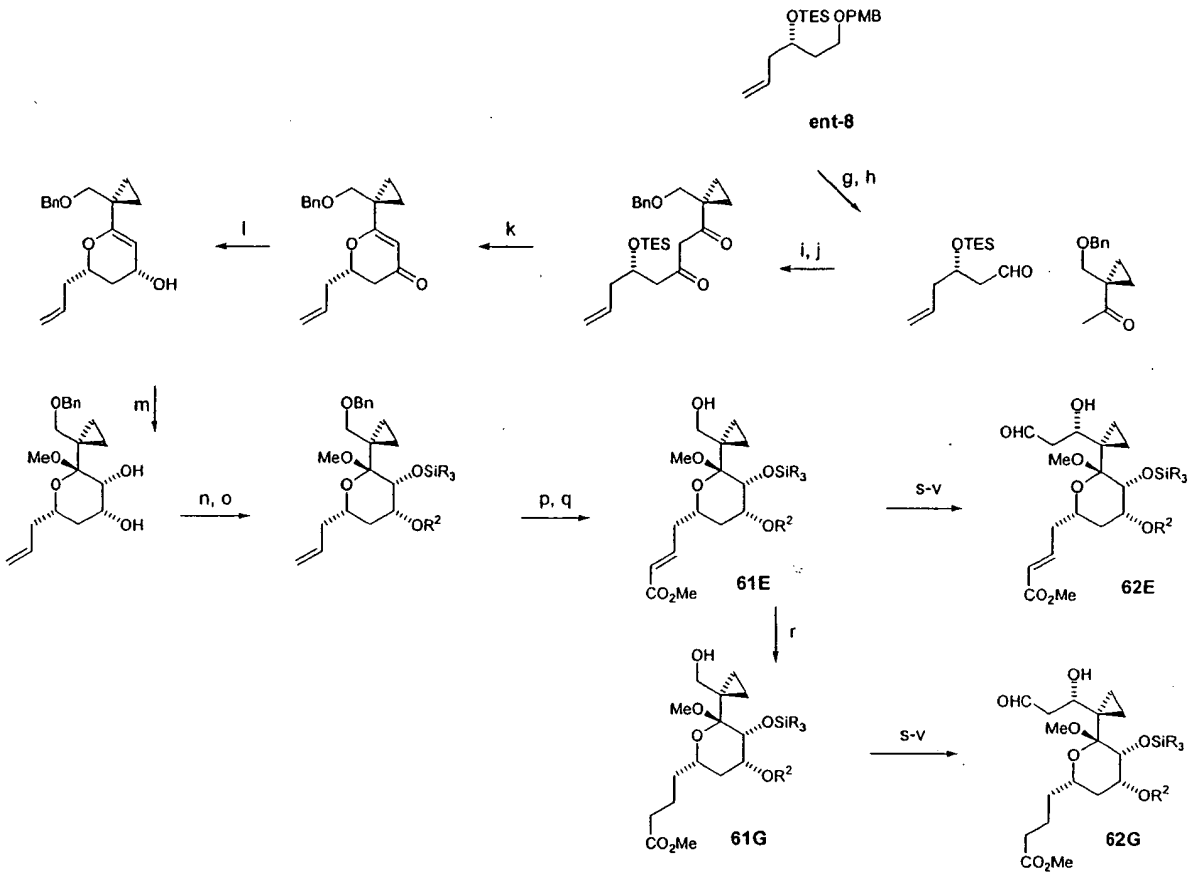
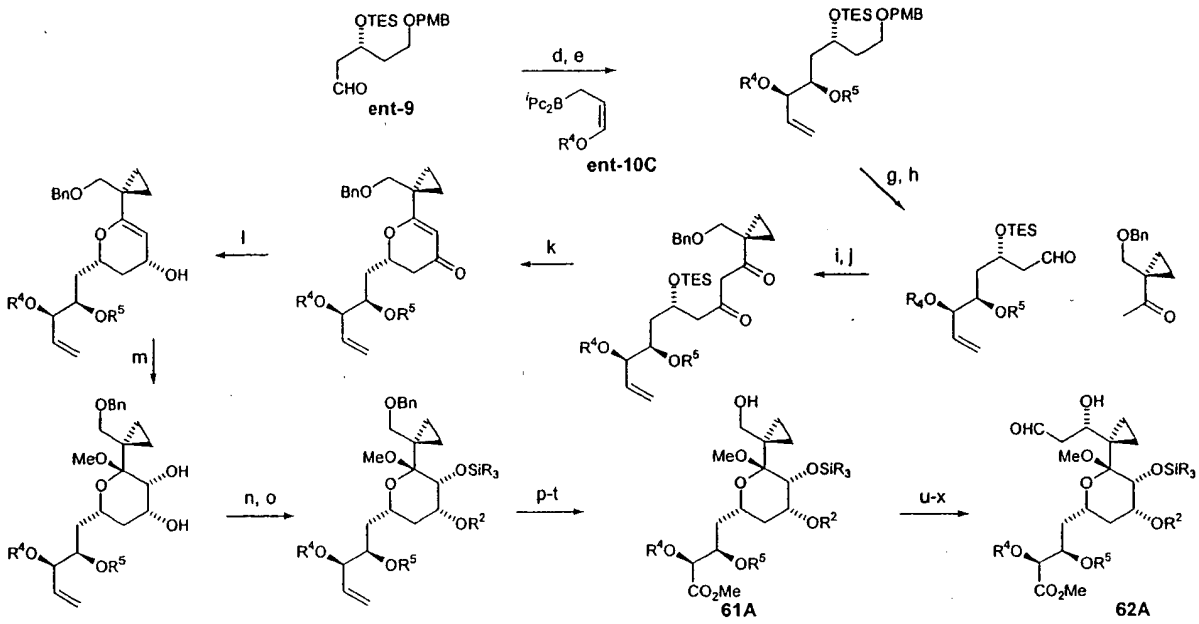

1. Oxidation to aldehyde (preferably py·SO3, Et3N, DMSO, CH2Cl2)
2. allylBEt2, Et2O
3. cat. OsO4, N-Me-morpholine N-oxide, t-BuOH/H2O
4. Pb(OAc)4, pyridine
61A,B,E-H
62A,B,E-H
62A,B,E-H
62C,D,I,J
63A-J
R2BO
R8
R2BOTf or R2BCl
Et3N or i-Pr2NEt
O
R8
1. Base, R3X (x = halide, OTf, other alkylating agents)
2. (S)-B-Me-CBS (20 equiv.), BH3 SMe2, CH2Cl2
3. aq. LiOH, THF
63A-J
64A-J
CBS = catalyst named after Corey, Bakshi, and Shibata
1. PPh3, DIAD, THF (0.05M), RT, 15 min, add 64A-J (0.003M in THF) via syringe pump
2. HF-pyridine, THF or aq. HCl, THF or other deprotection strategies compatible with nature of R2, R3, R4, R5
64A-J
65A-J

FIG. 83



Reagents and conditions: g) DDQ, CH_2Cl_2/H_2O; h) oxidation to aldehyde; i) LDA, THF, -78°C; j) oxidation to ketone; k) H^+; l) $NaBH_4$, $CeCl_3 \cdot 7H_2O$, MeOH; m) mCPBA, $NaHCO_3$, CH_2Cl_2/MeOH; n) base, R_2X; o) R_3SiOTf, 2,6-lutidine; p) LiDBB, THf or Li, naphtalene, THF; q) Ru-alkylidene catalyst (cross metathesis); r) conjugate reduction; s) oxidation to aldehyde; t) $allylBEt_2$; u) cat. OsO_4, NMO; v) $Pb(OAc)_4$ PMB = p-methoxybenzyl, TES = triethylsilyl, NMO = 4-methylmorpholine-N-oxide, DDQ = 2,3-dichloro-5,6-dicyano-1,4-benzoquinone, LDA = lithium diisopropylamide, mCPBA = m-chloroperbenzoic acid, Bn = benzyl.

FIG. 84

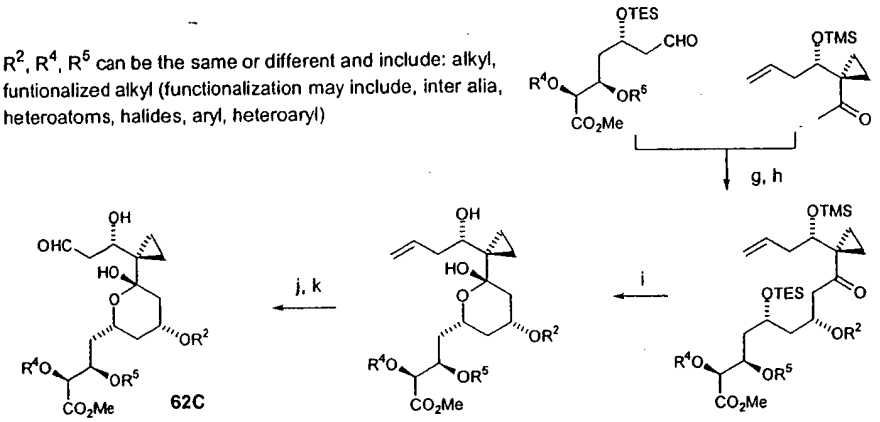


Reagents and conditions: d) **ent-10C** (prepared from $R^4OCH_2CH{=}CH_2$, sBuLi, THF, -78°C, 15 min, then (-)-Ipc$_2$BOMe, -78°C), then **ent-9**, -95°C, 30% H_2O_2, NaOH; e) base R_5X; g) DDQ, CH_2Cl_2/H_2O; h) oxidation to aldehyde; i) LDA, THF; j) oxidation to ketone; k) H^+; l) $NaBH_4$, $CeCl_3{\cdot}7H2O$, MeOH; m) mCPBA, $NaHCO_3$, CH_2Cl_2/MeOH; n) base, R_2X; o) TESOTf, 2,6-lutidine, CH_2Cl_2; p) cat. OsO_4, NMO, acetone/H_2O; q) $Pb(OAc)_4$, pyridine; r) $NaClO_2$, NaH_2PO_4, 2-Me-2-butene, tBuOH/H_2O; s) CH_2N_2; t) hydrogenolysis; u) oxidation to aldehyde; v) allylBEt$_2$; w) cat. OsO_4, NMO; x) $Pb(OAc)_4$. PMB = p-methoxybenzyl, TES = triethylsilyl, NMO = 4-methylmorpholine-N-oxide, Ipc = isopinocampheyl, DDQ = 2,3-dichloro-5,6-dicyano-1,4-benzoquinone, LDA = lithium diisopropylamide, mCPBA = m-chloroperbenzoic acid, Bn = benzyl.

R^2, R^4, R^5 can be the same or different and include: alkyl, funtionalized alkyl (functionalization may include, inter alia, heteroatoms, halides, aryl, heteroaryl)

FIG. 85

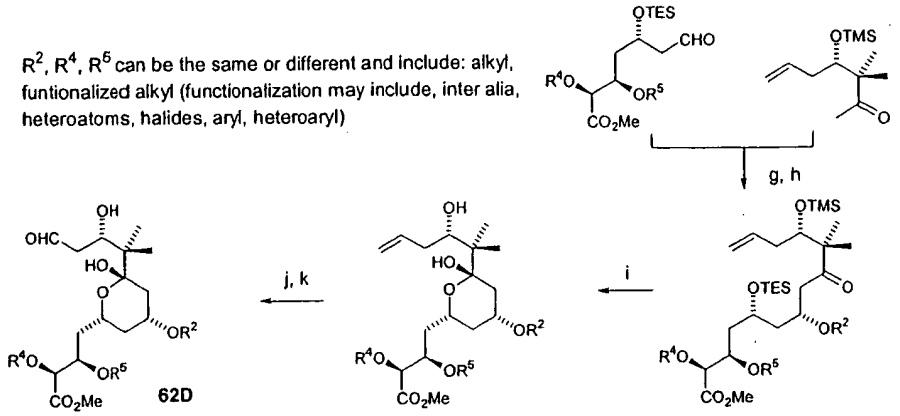
R^2, R^4, R^5 can be the same or different and include: alkyl, funtionalized alkyl (functionalization may include, inter alia, heteroatoms, halides, aryl, heteroaryl)



Reagents and conditions: g) LDA, THF; h) base R_5X; i) H^+; j) cat. OsO_4, NMO; k) $Pb(OAc)_4$. TMS = trimethylsilyl, TES = triethylsilyl, NMO = 4-methylmorpholine-N-oxide, LDA = lithium diisopropylamide.

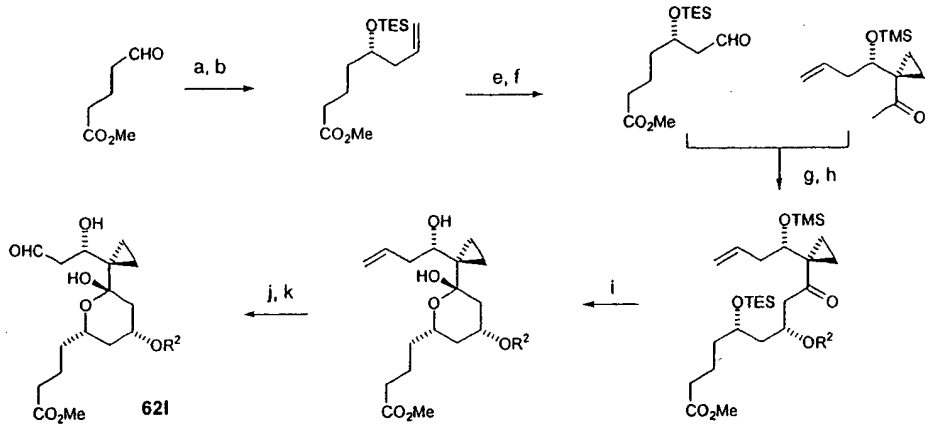
FIG. 86

R^2, R^4, R^5 can be the same or different and include: alkyl, funtionalized alkyl (functionalization may include, inter alia, heteroatoms, halides, aryl, heteroaryl)



Reagents and conditions: g) LDA, THF; h) base R_5X; i) H^+; j) cat. OsO_4, NMO; k) $Pb(OAc)_4$. TMS = trimethylsilyl, TES = triethylsilyl, NMO = 4-methylmorpholine-N-oxide, LDA = lithium diisopropylamide.

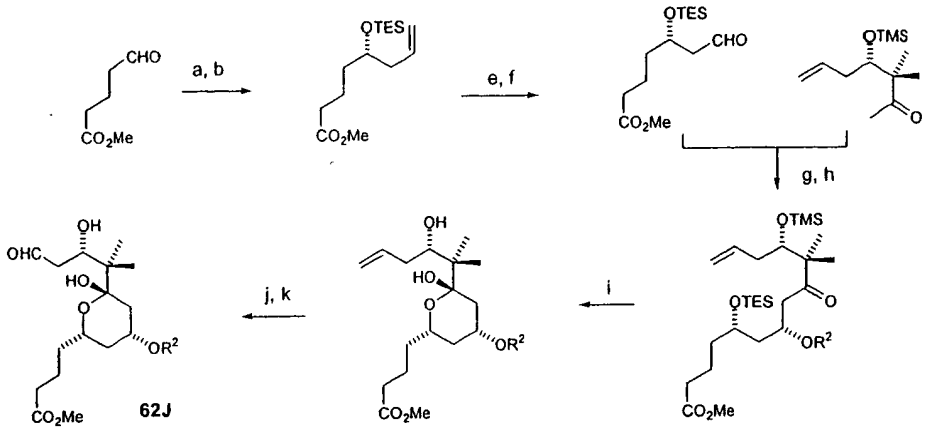
FIG. 87



Reagents and conditions: a) $Ipc_2Ballyl$; b)TESCl; c) cat. OsO_4, NMO; d) $Pb(OAc)_4$; d) LDA, THF; e) base R_5X; f) H^+; g) cat. OsO_4, NMO; h) $Pb(OAc)_4$. TMS = trimethylsilyl, TES = triethylsilyl, NMO = 4-methylmorpholine-N-oxide, LDA = lithium diisopropylamide.

R^2 can include: alkyl, funtionalized alkyl (functionalization may include, inter alia, heteroatoms, halides, aryl, heteroaryl)

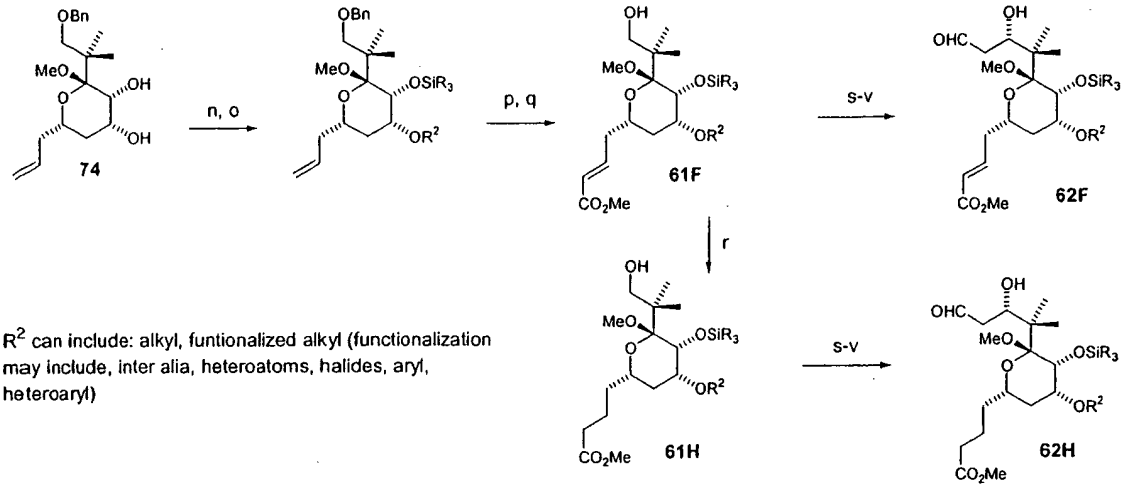
FIG. 88



Reagents and conditions: a) $Ipc_2Ballyl$; b)TESCl; c) cat. OsO_4, NMO; d) $Pb(OAc)_4$; d) LDA, THF; e) base R_5X; f) H^+; g) cat. OsO_4, NMO; h) $Pb(OAc)_4$. TMS = trimethylsilyl, TES = triethylsilyl, NMO = 4-methylmorpholine-N-oxide, LDA = lithium diisopropylamide.

R^2 can include: alkyl, funtionalized alkyl (functionalization may include, inter alia, heteroatoms, halides, aryl, heteroaryl)

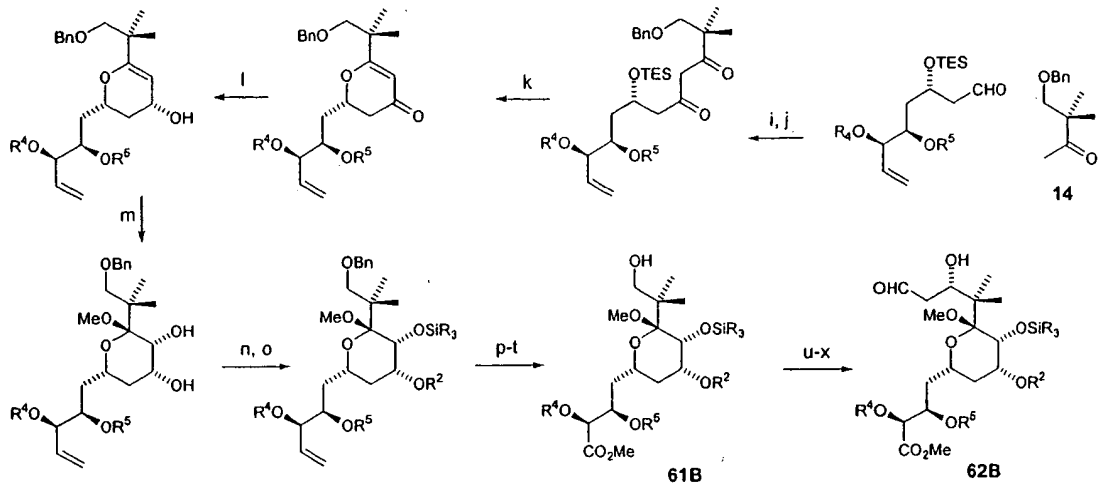
FIG. 89



R^2 can include: alkyl, funtionalized alkyl (functionalization may include, inter alia, heteroatoms, halides, aryl, heteroaryl)

Reagents and conditions: n) base, R_2X; o) TESOTf, 2,6-lutidine; p) LiDBB, THf or Li, naphtalene, THF; q) Ru-alkylidene catalyst (cross metathesis); r) conjugate reduction; s) oxidation to aldehyde; t) allylBEt_2; u) cat. OsO_4, NMO; v) $Pb(OAc)_4$ PMB = p-methoxybenzyl, TES = triethylsilyl, NMO = 4-methylmorpholine-N-oxide, DDQ = 2,3-dichloro-5,6-dicyano-1,4-benzoquinone, LDA = lithium diisopropylamide, mCPBA = m-chloroperbenzoic acid, Bn = benzyl.

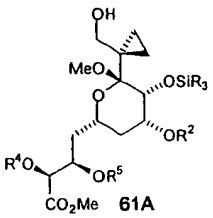
FIG. 90



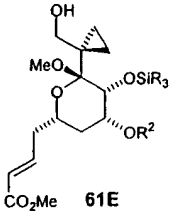
Reagents and conditions: i) LDA, THF; j) oxidation to ketone; k) H^+; l) $NaBH_4$, $CeCl_3 \cdot 7H2O$, MeOH; m) mCPBA, $NaHCO_3$, CH_2Cl_2/MeOH; n) base, R_2X; o) TESOTf, 2,6-lutidine, CH_2Cl_2; p) cat. OsO_4, NMO, acetone/H_2O; q) $Pb(OAc)_4$, pyridine; r) $NaClO_2$, NaH_2PO_4, 2-Me-2-butene, tBuOH/H_2O; s) CH_2N_2; t) hydrogenolysis; u) oxidation to aldehyde; v) allylBEt$_2$; w) cat. OsO_4, NMO; x) $Pb(OAc)_4$. PMB = p-methoxybenzyl, TES = triethylsilyl, NMO = 4-methylmorpholine-N-oxide, DDQ = 2,3-dichloro-5,6-dicyano-1,4-benzoquinone, LDA = lithium diisopropylamide, mCPBA = m-chloroperbenzoic acid, Bn = benzyl.

R^2, R^4, R^5 can be the same or different and include: alkyl, funtionalized alkyl (functionalization may include, inter alia, heteroatoms, halides, aryl, heteroaryl)

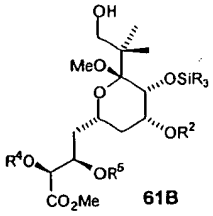
FIG. 91



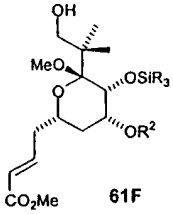
61A



61E

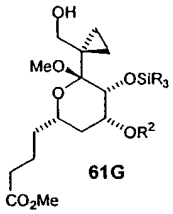


61B

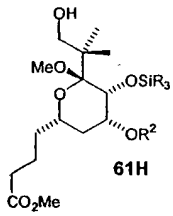


61F

R^2, R^4, R^5 can be the same or different and include: alkyl, funtionalized alkyl (functionalization may include, inter alia, heteroatoms, halides, aryl, heteroaryl)

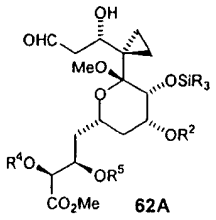


61G

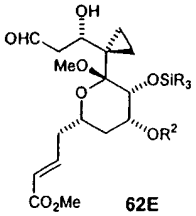


61H

FIG. 92

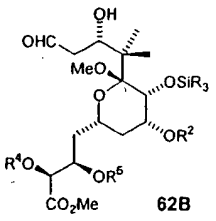


62A

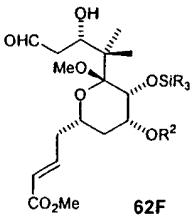


62E

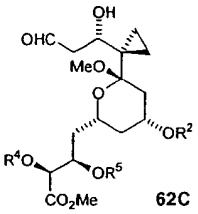
R^2, R^4, R^5 can be the same or different and include: alkyl, funtionalized alkyl (functionalization may include, inter alia, heteroatoms, halides, aryl, heteroaryl)



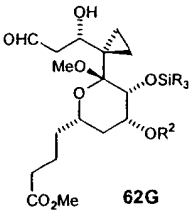
62B



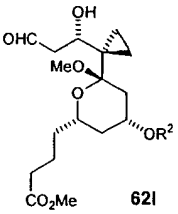
62F



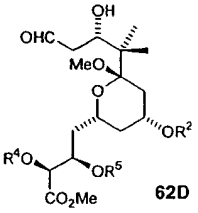
62C



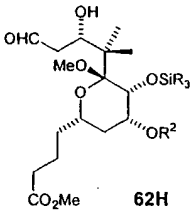
62G



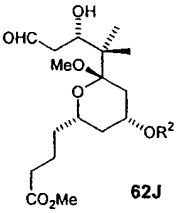
62I



62D

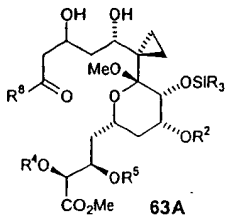


62H

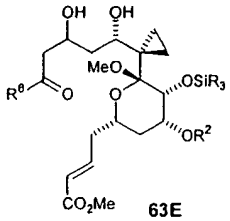


62J

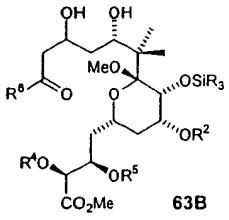
FIG. 93



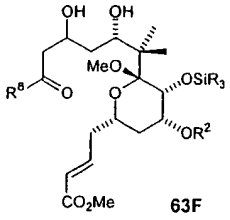
63A



63E

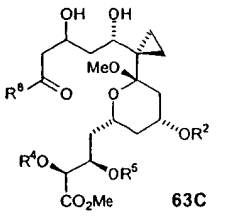


63B

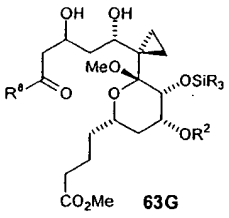


63F

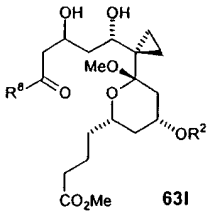
R^2, R^4, R^5 can be the same or different and include: alkyl, funtionalized alkyl (functionalization may include, inter alia, heteroatoms, halides, aryl, heteroaryl), and where R^8 = aryl, heteroaryl, alkyl, functionalized alkyl, alkenyl, functionalized alkenyl, alkynyl, functionalized alkynyl (functionalization may include, inter alia, heteroatoms, halides, aryl, heteroaryl).



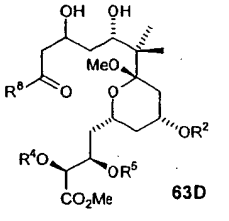
63C



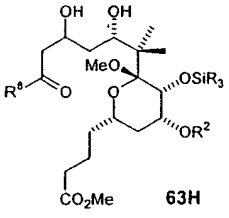
63G



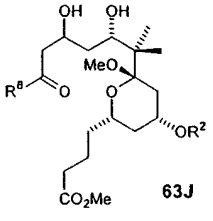
63I



63D

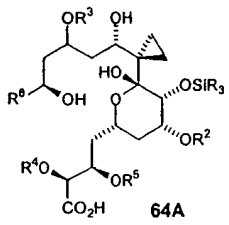


63H

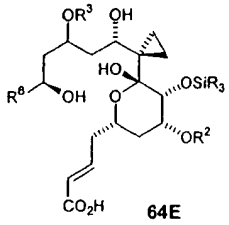


63J

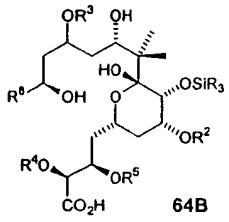
FIG. 94



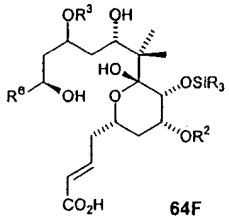
64A



64E

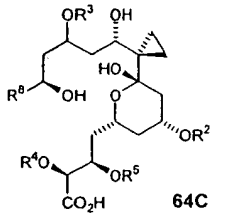


64B

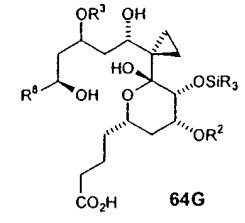


64F

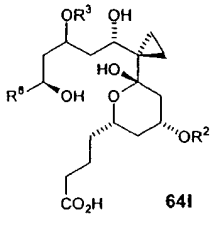
R^2, R^3, R^4, R^5 can be the same or different and include: alkyl, funtionalized alkyl (functionalization may include, inter alia, heteroatoms, halides, aryl, heteroaryl), and where R^6 = aryl, heteroaryl, alkyl, functionalized alkyl, alkenyl, functionalized alkenyl, alkynyl, functionalized alkynyl (functionalization may include, inter alia, heteroatoms, halides, aryl, heteroaryl). The configuration at the carbon bearing the OR^3 substituent can have the *R*- or *S*-configuration



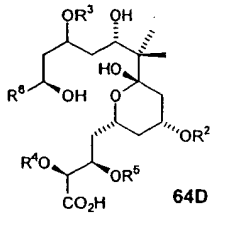
64C



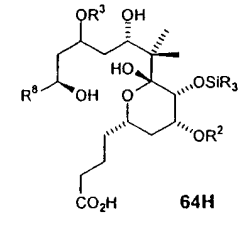
64G



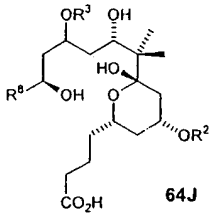
64I



64D

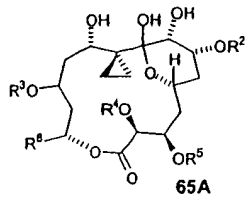


64H

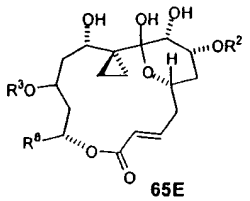


64J

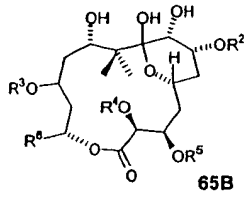
FIG. 95



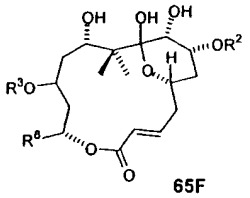
65A



65E

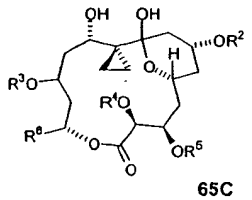


65B

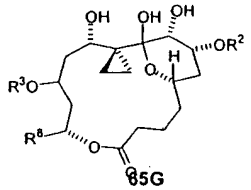


65F

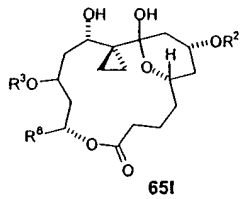
R^2, R^3, R^4, R^5 can be the same or different and include: H, alkyl, funtionalized alkyl (functionalization may include, inter alia, heteroatoms, halides, aryl, heteroaryl), and where R^8 = aryl, heteroaryl, alkyl, functionalized alkyl, alkenyl, functionalized alkenyl, alkynyl, functionalized alkynyl (functionalization may include, inter alia, heteroatoms, halides, aryl, heteroaryl). The configuration at the carbon bearing the OR^3 substituent can have the *R*- or *S*-configuration



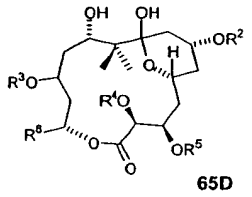
65C



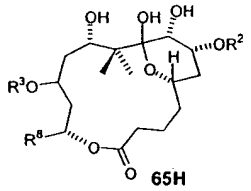
65G



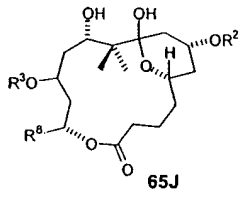
65I



65D



65H



65J

FIG. 96

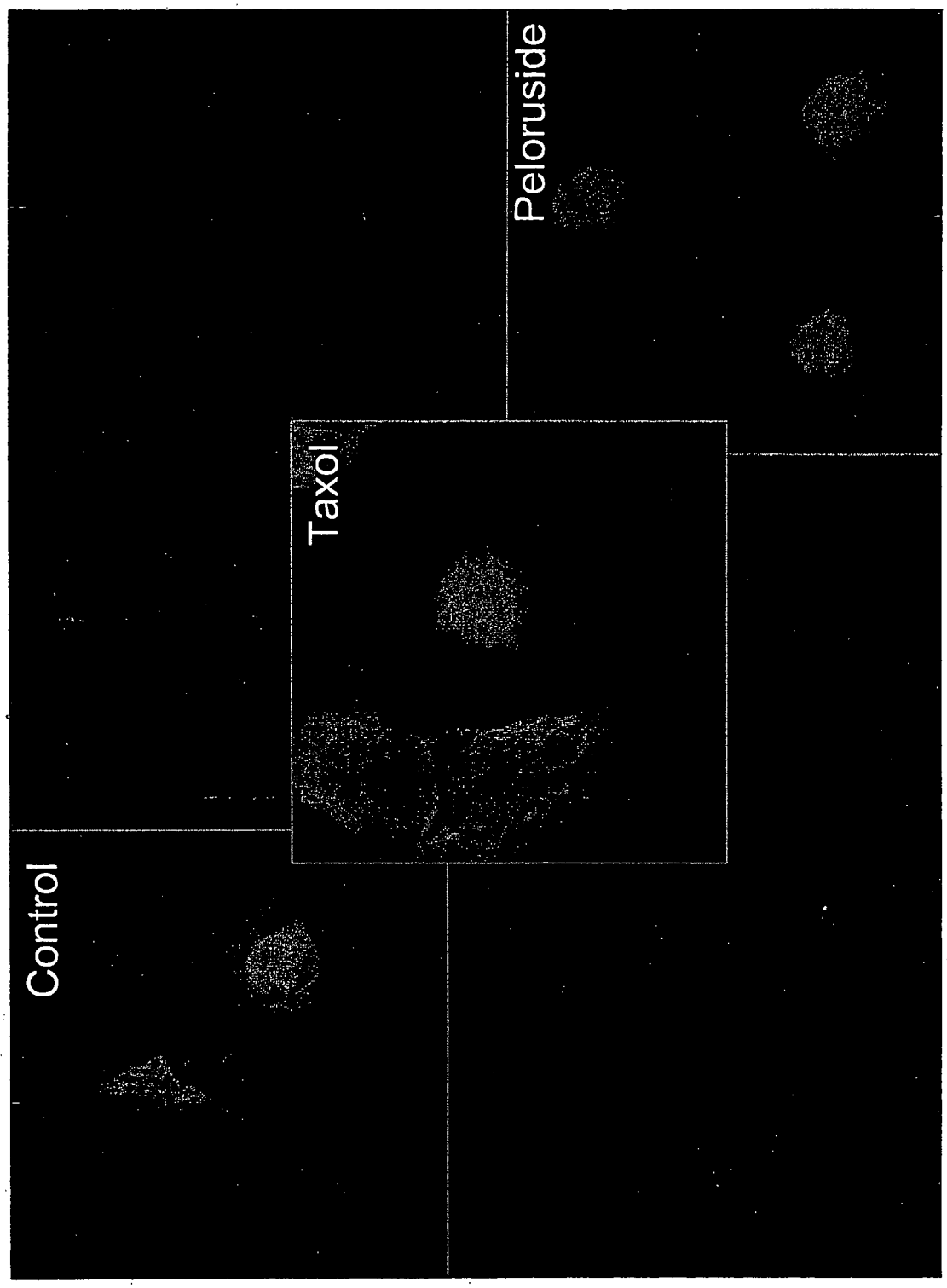


FIG. 97